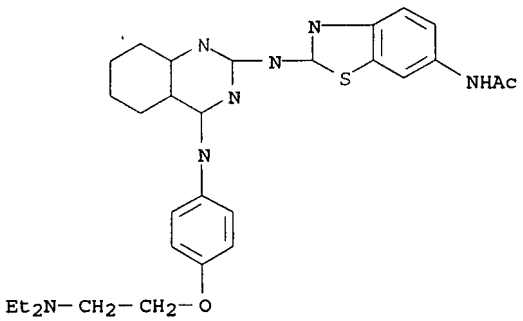
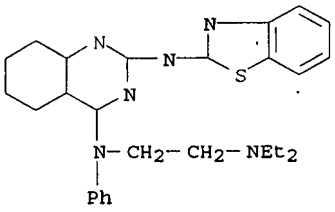


● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride (5CI) (CA INDEX NAME)



● HCl

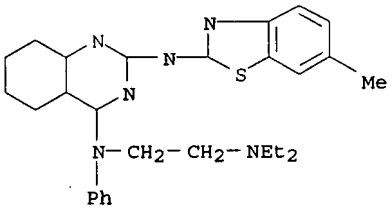
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L29 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1953:12393 HCAPLUS
DN 47:12393
OREF 47:2217c-e
TI Vitamin B6 derivatives
IN Heyl, Dorothea
PA Merck & Co., Inc.
DT Patent
LA Unavailable
FAN.CNT 1

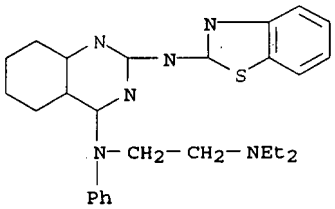
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US---2583774		19520129	1948US-0024412	19480430 <--

AB The acetoxime of 3-acetoxy-5-acetoxymethyl-4-formyl-2-methylpyridine (I), m. 114.5-15°, refluxed 2 h. with Ac2O, gives the 4-cyano analog (II) of I, m. 63-4°. II, refluxed 2 h. in EtOH containing 0.1% Na, gives the 3-HO analog (III) of II, m. 209-10°. III with 3 N KOH gives 4-carboxy-3-hydroxy-5-hydroxymethyl-2-methylpyridine (IV), m. 253-4° (decomposition). IV, refluxed with EtOH containing anhydrous HCl, gives the lactone of IV, m. 273-3.5° (decomposition). Alternatively, 5-chloromethyl-4-cyano-3-hydroxy-2-methylpyridine, m. 167-8° (decomposition), is hydrolyzed to 4-carbamyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine-HCl, m. 210-11° (decomposition), which in turn gives IV. The lactone has growth-promoting and antianemia activity. Cf. C.A. 44, 10740c.
IT **873407-61-5P**, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- **873407-64-8P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- **879676-37-6P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride

RL: PREP (Preparation)
(preparation of)
RN 873407-61-5 HCAPLUS
CN Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 873407-64-8 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-(5CI) (CA INDEX NAME)



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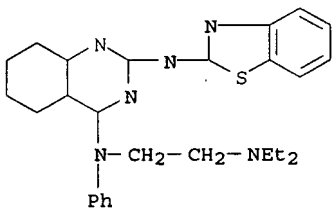
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride (5CI) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L29 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1953:3470 HCAPLUS
DN 47:3470
OREF 47:617b-h
TI Heterocyclically substituted diaminoquinazolines
PA C I B A Ltd.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB----664262		19520102	1949GB-0003339	19490207 <--

AB 2,4-Diaminoquinazolines substituted by a thiazolyl or imidazolyl group on one of the NH2 groups and by a dialkylaminoalkyl group on the other, prepared by standard methods, are useful as medicinals, some being antituberculars. 2-(Substituted amino)-4-(2-diethylaminoethylamino)quinaz

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=> b reg
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DICTIONARY FILE UPDATES:  14 AUG 2007  HIGHEST RN 944643-48-5

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L11              STR
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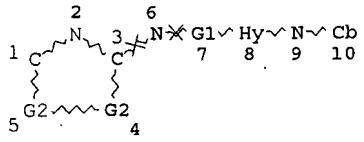


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DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E8 C  E2 N  AT   8

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NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
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FILE LAST UPDATED: 14 Aug 2007 (20070814/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L26 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:565407 HCAPLUS
DN 147:9943
TI Diarylamines as ErbB inhibitors, their preparation, pharmaceutical compositions, and use in therapy
IN **Lyssikatos, Joseph P.**; Marmsater, Fredrik P.; **Zhao, Qian**; Greschuk, Julie Marie
PA **Array Biopharma**, Inc., USA
SO PCT Int. Appl., 173pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO2007059257	A2	20070524	2006WO-US44431	20061115

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI 2005US-736289P P 20051115
2006US-817019P P 20060628
OS MARPAT 147:9943
GI

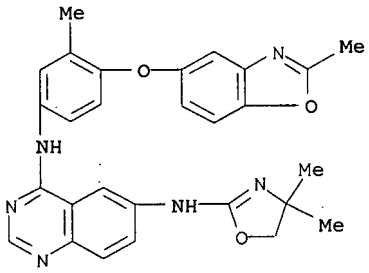
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to diarylamine compds. of formula I, which are inhibitors of epidermal growth factor receptor (ErbB). In compds. I, Y is N or C-CN; A is O, C(O), S, SO, or SO2; E is (un)substituted bicyclic nitrogen-containing heteroaryl; R1 is H or alkyl; n is 0-4; each R2 is independently selected from halo, cyano, nitro, alkyl, trifluoromethyl, difluoromethyl, fluoromethyl fluoromethoxy, azido, alkylthio, alkoxy, acyl, alkoxycarbonyl, etc.; and R3 and R4, together with the carbon atoms to which they are attached, form a substituted fused Ph ring or a substituted fused 5- or 6-membered heteroaryl ring; including pharmaceutically acceptable salts thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable diluent or carrier, as well as to the use of the compns. for the treatment of hyperproliferative diseases, such as cancer and inflammation. Substitution of 2-chloro-4-nitropyridine with benzyl alc. followed by substitution with hydrazine, heterocyclization with tri-Me orthoformate, and hydrogenation gave triazolopyridinol II, which underwent substitution of 1-fluoro-2-methyl-4-nitrobenzene and hydrogenation to form aniline III. Condensation of 2-amino-5-nitrobenzonitrile with DMF di-Me acetal followed by hydrogenation, addition to thiocarbonyldiimidazole, and substitution with 2-amino-2-methylpropan-1-ol resulted in the formation of thiourea IV, which was cyclized with aniline III and cyclized to the oxazoline with tosyl chloride to give diarylamine V. The compds. of the invention, e.g., V, are inhibitors of ErbB (no data).
IT **937263-22-4P 937263-27-9P 937263-28-0P**
937263-29-1P 937263-30-4P 937263-31-5P

937263-32-6P 937263-33-7P 937263-34-8P
937263-37-1P 937263-43-9P 937263-45-1P
937263-49-5P 937263-50-8P 937263-61-1P
937263-62-2P 937263-77-9P 937263-78-0P
937263-79-1P 937263-81-5P 937263-93-9P
937264-33-0P 937264-55-6P 937264-82-9P
937264-92-1P 937265-13-9P 937266-01-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of diarylamines as ErbB inhibitors)

IT **937263-22-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of diarylamines as ErbB inhibitors)

RN 937263-22-4 HCAPLUS
CN 4,6-Quinazolinediamine, N6-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-N4-[3-methyl-4-[(2-methyl-5-benzoxazolyl)oxy]phenyl]- (CA INDEX NAME)



L26 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:409232 HCAPLUS
DN 142:463739
TI Preparation of quinazoline analogs as type I receptor tyrosine kinase inhibitors
IN **Wallace, Eli; Topalov, George; Lyssikatos, Joseph; Buckmelter, Alexandre; Zhao, Qian**
PA USA
SO U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US2005101616	A1	20050512	2003US-0642440	20030814 <--
AU2004264937	A1	20050224	2004AU-0264937	20040810 <--
CA---2535614	A1	20050224	2004CA-2535614	20040810 <--
US2005043334	A1	20050224	2004US-0914974	20040810 <--
WO2005016346	A1	20050224	2004WO-US26235	20040810 <--
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP---1660090	A1	20060531	2004EP-0780990	20040810 <--
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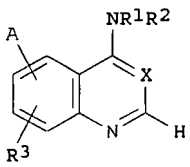
CN---1852714	A	20061025	CN 2004-80026458	20040810 <--
JP2007502295	T	20070208	2006JP-0523384	20040810 <--
MX2006PA01767	A	20060512	2006MX-PA01767	20060214 <--

	NO2006001171	A	20060410	2006NO-0001171	20060313 <--
PRAI	2003US-0642440	A	20030814	<--	
	2004US-551718P	P	20040310		
	2004WO-US26235	W	20040810		

OS MARPAT 142:463739

GI



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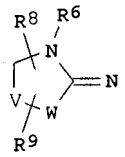

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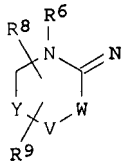

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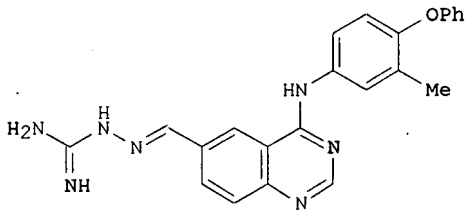


IV

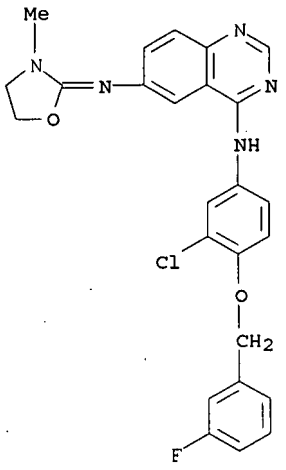
AB The title compds. I [A group is bonded to at least one of the carbons at the 5, 6, 7 or 8 position of the bicyclic ring, and the ring is substituted by up to three independent R3 groups; X = N, CH, CF, C(CN); R1 = (un)substituted monocyclic or bicyclic aryl or heteroaryl; R2 = H, (un)substituted alkyl; R3 = H, halo, CN, NO2; A = CH:NN(R8)C(:NR6)NR6R8, UnZ; n = 0-1; U = (un)substituted alkyl, alkenyl, alkynyl; Z = II, III; W, V and Y = CR7R8, CR8R9, O, NR6, S, SO, SO2; R6, R8, R9 = H, CF3, alkyl, etc.; with provisos], useful as type I receptor tyrosine kinase inhibitors and for the treatment of hyperproliferative diseases such as cancer, were prepared Thus, reacting 4-(3-methyl-4-phenoxyphenylamino)quinazoline-6-carboxaldehyde with hydrazinecarboximidamide in the presence of 1 drop of concentrate HCl in MeOH afforded 68% IV. The compds. I have IC50's from less than 1 nM to 50 μM in EGFR/ErbB2 assays.

IT **851545-54-5P 851545-55-6P 851545-56-7P**
851545-57-8P 851545-58-9P 851545-59-0P
851545-60-3P 851545-61-4P 851545-62-5P
851545-63-6P 851545-64-7P 851545-65-8P
851545-66-9P 851545-67-0P 851545-68-1P
851545-69-2P 851545-70-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline analogs as type I receptor tyrosine kinase inhibitors for treating hyperproliferative diseases such as cancer)

IT **851545-54-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline analogs as type I receptor tyrosine kinase inhibitors for treating hyperproliferative diseases such as cancer)

RN 851545-54-5 HCAPLUS

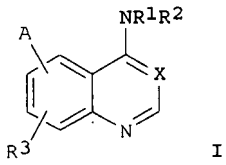
CN 4,6-Quinazolinediamine, N4-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-N6-(3-methyl-2-oxazolidinylidene)- (9CI) (CA INDEX NAME)



L26 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:160839 HCAPLUS
DN 142:240462
TI Preparation of aminoquinazolines as receptor tyrosine kinase inhibitors
IN **Wallace, Eli**; **Topalov, George**; **Lyssikatos, Joseph**; **Buckmelter, Alexandre**; **Zhao, Qian**
PA USA
SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 642,440.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2005043334	A1	20050224	2004US-0914974	20040810 <--
	US2005101616	A1	20050512	2003US-0642440	20030814 <--
PRAI	2003US-0642440	A2	20030814	<--	
	2004US-551718P	P	20040310		

OS MARPAT 142:240462
GI



I

AB Title compds. I [A = Q, Z; Q = N-acetamidinoimine; X = N, CH, etc.; Z = dihydroimidazole, etc.; R1 = (hetero)aryl, etc.; R2 = H, alkyl, allyl, etc.; R3 = H, halo, CN, NO2, etc.] are prepared For instance, (E)-N-[[[4-((3-methyl-4-phenoxyphenyl)amino)quinazolin-6-yl]methylene]amino]-2-methoxyacetamidine is prepared in two steps from 4-((3-methyl-4-phenoxyphenyl)amino)quinazoline-6-carboxaldehyde, hydrazine and 2-methoxyacetimidic acid Me ester. Compds. of the invention exhibit IC50 values in the range of 1 - 50 nM for ErbB-2 tyrosine kinase. I are useful for the treatment of hyperproliferative diseases such as cancer.
IT **845271-76-3P**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845271-77-4P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845271-79-6P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(3-oxa-1,8-diazaspiro[4.5]dec-1-en-2-yl)amino]quinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

IT **845271-69-4P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-72-9P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845271-74-1P**, 4-[[3-Chloro-4-(3-fluorobenzyloxy)phenyl]amino]-6-[(3,8-dioxa-1-azaspiro[4.5]dec-1-en-2-yl)amino]quinazoline **845271-75-2P**, 6-[(3,8-Dioxa-1-azaspiro[4.5]dec-1-en-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-78-5P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazol-5-yl]ethanone **845271-81-0P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3-oxa-1,8-diazaspiro[4.5]dec-1-en-8-yl]ethanone **845271-82-1P**, 6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-83-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(1-oxa-3,8-diazaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-85-4P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-en-8-yl]ethanone **845271-87-6P**, [4-Methyl-2-[[4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]methanol **845271-88-7P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-89-8P**, 6-[(1,8-Dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-90-1P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-91-2P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-92-3P**, 6-[(5,5-Dimethyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-93-4P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-94-5P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-95-6P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-96-7P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-97-8P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845271-98-9P**, rel-(1R)-1-[(5S)-5-Methyl-2-[[4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-5-yl]ethanol **845271-99-0P**, 6-[(4,5-Dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-00-6P**, [2-[[4-((3-Chloro-4-((pyridin-2-yl)methoxy)phenyl)amino)quinazolin-6-yl]amino]-4-methyl-4,5-dihydrooxazol-4-yl]methanol **845272-01-7P**, rel-(1R)-1-[(5S)-2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-5-methyl-4,5-dihydrooxazol-5-yl]ethanol **845272-02-8P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,4-dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-03-9P**, rel-(1R)-1-[(5S)-2-[[4-[[4-[(3-Fluorobenzyl)oxy]-3-chlorophenyl]amino]quinazolin-6-yl]amino]-5-methyl-4,5-dihydrooxazol-5-yl]ethanol **845272-04-0P**, 6-[(5-Methyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-05-1P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-06-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845272-07-3P**, 6-[(4-Methyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-08-4P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845272-09-5P**, 4-[[3-Methyl-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845272-10-8P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-11-9P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-12-0P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,5,6,6a-

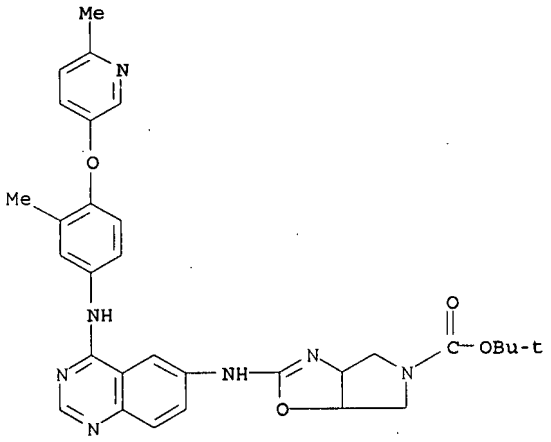
tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845272-14-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845272-16-4P**, [2-[[4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4-methyl-4,5-dihydrooxazol-4-yl]methanol **845272-17-5P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(6-oxa-4-azaspiro[2.4]hept-4-en-5-yl)amino]quinazoline **845272-18-6P**, [2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-4-hydroxymethyl-4,5-dihydrooxazol-4-yl]methanol **845272-19-7P**, (1R)-1-[(4S)-2-[[4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]ethanol **845272-21-1P**, (R)-4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-22-2P**, (S)-4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-23-3P**, (S)-4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-24-4P**, (R)-4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-25-5P**, 4-[[4-[(5-Chloropyridin-3-yl)oxy]-3-methylphenyl]amino]-6-[(4,4-dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-26-6P**, 4-[[3-Methyl-4-[(pyridin-3-yl)oxy]phenyl]amino]-6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-27-7P**, 4-[[4-[(5-Fluoropyridin-3-yl)oxy]-3-methylphenyl]amino]-6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-30-2P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)(methyl)amino]quinazoline **845272-32-4P**, [2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]methanol
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

IT **845271-80-9**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3-oxa-1,8-diazaspiro[4.5]dec-1-ene-8-carboxylic acid tert-butyl ester **845271-84-3**, 2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-ene-8-carboxylic acid tert-butyl ester **845271-86-5**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-ene-8-carboxylic acid tert-butyl ester **845272-13-1**, 2-[[4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845272-15-3**, 2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845272-20-0**, 6-[[(4S)-4-((1R)-1-(tert-Butoxy)ethyl)-4,5-dihydrooxazol-2-yl]amino]-4-[[3-chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quinazoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

IT **845271-76-3P**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

RN 845271-76-3 HCAPLUS

CN 5H-Pyrrolo[3,4-d]oxazole-5-carboxylic acid, 3a,4,6,6a-tetrahydro-2-[[4-[[3-methyl-4-[(6-methyl-3-pyridinyl)oxy]phenyl]amino]-6-quinazolinyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



=> d bib abs hitstr l29 tot

L29 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:875260 HCAPLUS
DN 139:364951
TI Preparation of quinazoline derivatives as antipruritic agents
IN Okano, Masahiko; Oyama, Tatsuya
PA Nippon Shinyaku Co., Ltd., Japan
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003091224	A1	20031106	2003WO-JP05432	20030428 <--
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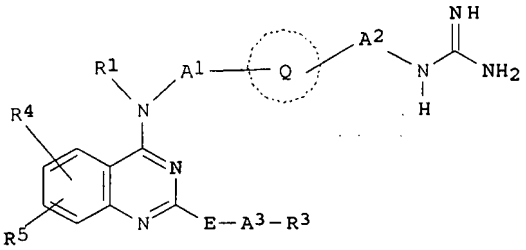
	CN---1659150	A	20050824	2003CN-0812905	20030428 <--
	MX2004PA10539	A	20050125	2004MX-PA10539	20041025 <--
PRAI	2002JP-0125452	A	20020426 <--		
	2002JP-0272314	A	20020918 <--		
	2002JP-0373400	A	20021225 <--		
	2003WO-JP05432	W	20030428 <--		

OS MARPAT 139:364951
GI



I

AB The title compds. I [R1 represents hydrogen or alkyl; ring Q represents cyclohexylene or phenylene; A1 and A2 each represents a single bond or alkylene; E represents NHCO, etc.; A3 represents a single bond, a divalent (un)saturated aliphatic hydrocarbon group, etc.; R3 represents a noncyclic aliphatic hydrocarbon group, etc.; and R4 and R5 are the same or different and each represents hydrogen, alkyl, etc.] are prepared In an in vitro test for binding to the nociceptin receptors, compds. of this invention showed the Ki values of 0.00014 μM to 0.00067 μM. Formulations are given.

IT **620953-35-7P 620953-79-9P 620955-73-9P 620955-97-7P 620956-60-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as antipruritic agents)

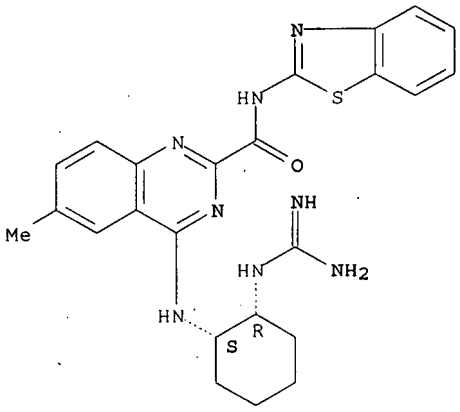
RN 620953-35-7 HCAPLUS

CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-N-2-benzothiazolyl-6-methyl-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

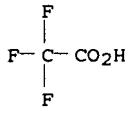
CRN 620953-34-6
CMF C24 H26 N8 O S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

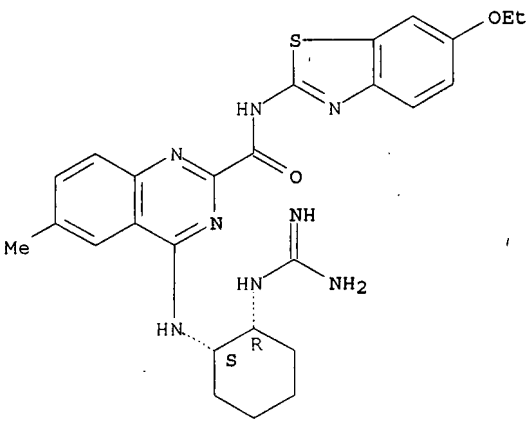


RN 620953-79-9 HCAPLUS
CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-N-(6-ethoxy-2-benzothiazolyl)-6-methyl-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

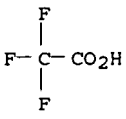
CRN 620953-78-8
CMF C26 H30 N8 O2 S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

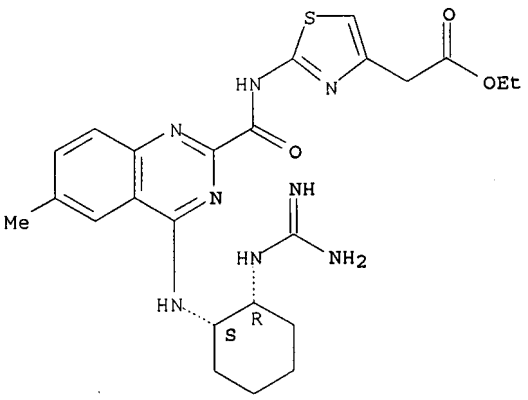


RN 620955-73-9 HCAPLUS
CN 4-Thiazoleacetic acid, 2-[[[4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-2-quinazolinyl]carbonyl]amino]-, ethyl ester, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

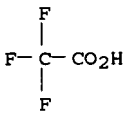
CRN 620955-72-8
CMF C24 H30 N8 O3 S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

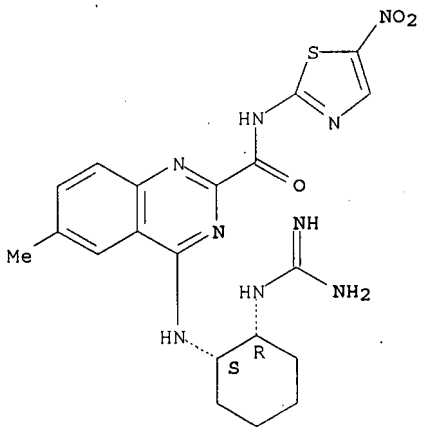


RN 620955-97-7 HCAPLUS
CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-N-(5-nitro-2-thiazolyl)-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

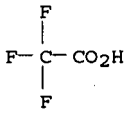
CRN 620955-96-6
CMF C20 H23 N9 O3 S

Relative stereochemistry.



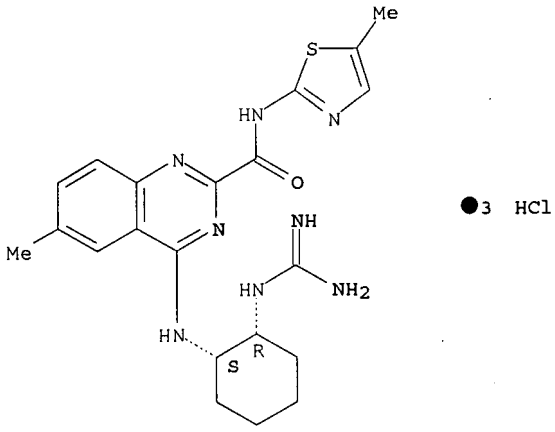
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 620956-60-7 HCAPLUS
CN 2-Quinazolinecarboxamide, 4-[[(1S,2R)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-N-(5-methyl-2-thiazolyl)-, trihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:757702 HCAPLUS
DN 139:255407
TI Azolylaminoazine compounds as inhibitors of protein kinases, and their therapeutic use
IN Binch, Hayley; Charrier, Jean-Damien; Everitt, Simon; Golec, Julian M. C.; Kay, David; Knegtel, Ronald; Miller, Andrew; Pierard, Francoise; Bebbington, David
PA Vertex Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003078426	A1	20030925	2003WO-US07904	20030314 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU2003225800	A1	20030929	2003AU-0225800	20030314 <--
	US2004002496	A1	20040101	2003US-0389709	20030314 <--
	US---7179826	B2	20070220		
	EP---1485381	A1	20041215	2003EP-0744682	20030314 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	2002US-364840P	P	20020315 <--		
	2003WO-US07904	W	20030314 <--		

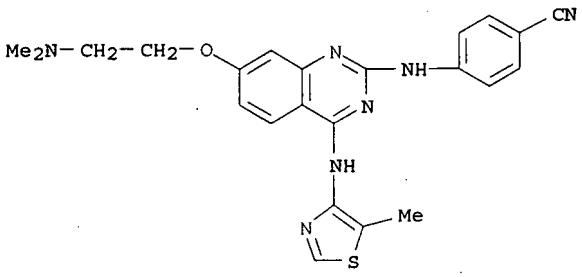
OS MARPAT 139:255407

AB The invention provides azolylaminoazine compds. useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compns. comprising the compds. and methods of using the compns. in the treatment of various diseases, conditions, and disorders.

IT **603932-31-6 603932-32-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azolylaminoazine compds. as inhibitors of protein kinases, therapeutic use, and use with other agents)

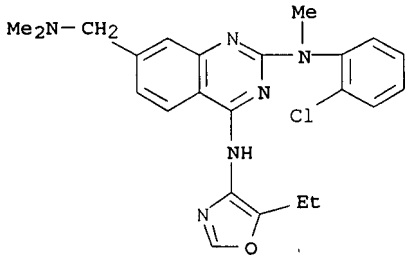
RN 603932-31-6 HCAPLUS

CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-methyl-4-thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



RN 603932-32-7 HCAPLUS

CN 2,4-Quinazolinediamine, N2-(2-chlorophenyl)-7-[(dimethylamino)methyl]-N4-(5-ethyl-4-oxazolyl)-N2-methyl- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:757700 HCAPLUS

DN 139:276913

TI Preparation of thiazolylaminopyrimidines and related compounds as inhibitors of protein kinases

IN Bebbington, David

PA Vertex Pharmaceuticals, Inc., USA; Binch, Hayley; Charrier, Jean-Damien; Everitt, Simon; Golec, Julian M. C.; Kay, David; Knegtel, Ronald; Miller, Andrew; Pierard, Francoise; et al.

SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2

DT Patent

LA English

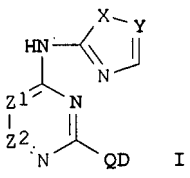
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2003078423	A1	20030925	2003WO-US07958	20030314 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU2003220300 A1 20030929 2003AU-0220300 20030314 <--
US2003225073 A1 20031204 2003US-0389707 20030314 <--
US---6846928 B2 20050125
EP---1485376 A1 20041215 2003EP-0716598 20030314 <--
EP---1485376 B1 20070627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
AT----365733 T 20070715 2003AT-0716598 20030314 <--
PRAI 2002US-364842P P 20020315 <--
2003WO-US07958 W 20030314 <--
OS MARPAT 139:276913
GI



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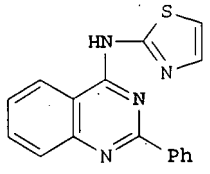
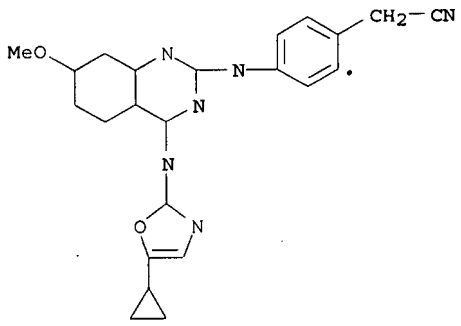


II

AB Title compds. I [X = O, S, (un)substituted NH; Y = N, (un)substituted CH; one of Z1 and Z2 = (un)substituted CH, the other is N; Q = (un)substituted NH, CH2, S, O, bond; D = aryl, heteroaryl] were prepared for use as inhibitors of GSK-3, Aurora-2, or Src protein kinases (no data). Thus, the quinazoline II was obtained by chlorinating 4-quinazolinone and reaction with 2-aminothiazole.

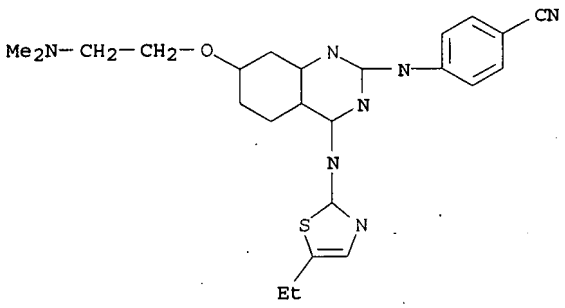
IT **606092-42-6P 606092-43-7P 606092-57-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolylaminopyrimidines and related compds. as inhibitors of protein kinases)

RN 606092-42-6 HCAPLUS
CN Benzeneacetonitrile, 4-[[4-[(5-cyclopropyl-2-oxazolyl)amino]-7-methoxy-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

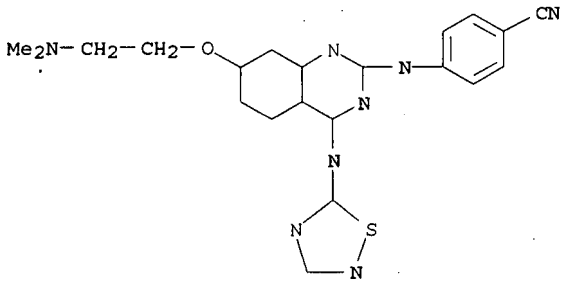


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 606092-43-7 HCAPLUS
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-ethyl-2-thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 606092-57-3 HCAPLUS
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-(1,2,4-thiadiazol-5-ylamino)-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

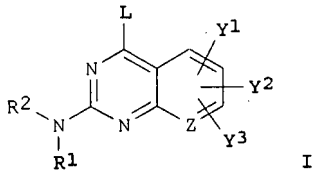
L29 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:977603 HCAPLUS
DN 138:55973
TI Preparation of quinazoline and pyrido[2,3-d]pyrimidine inhibitors of phosphodiesterase (PDE) 7
IN Pitts, William J.; Barbosa, Joseph
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2002102315	A2	20021227	2002WO-US19130	20020617 <--
	WO2002102315	A3	20031120		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA---2450724	A1	20021227	2002CA-2450724	20020617 <--
	US2003092721	A1	20030515	2002US-0173322	20020617 <--
	US---7022849	B2	20060404		
	US2003100571	A1	20030529	2002US-0173530	20020617 <--
	US---6838559	B2	20050104		
	EP---1404337	A2	20040407	2002EP-0742138	20020617 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

	JP2005506961	T	20050310	2003JP-0504904	20020617 <--
	US2006116516	A1	20060601	2005US-0281246	20051117 <--
PRAI	2001US-299287P	P	20010619	<--	
	2002US-368752P	P	20020329	<--	
	2002US-0173322	A3	20020617	<--	
	2002WO-US19130	W	20020617	<--	

OS MARPAT 138:55973

GI



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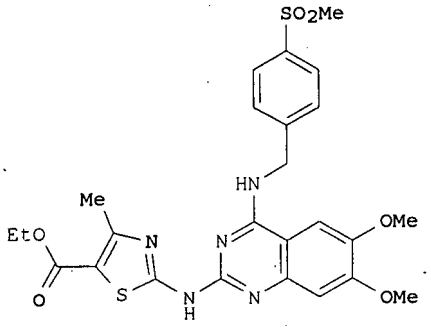


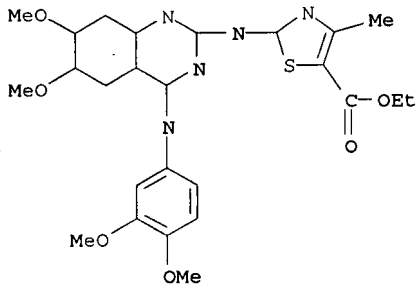
II

AB The title compds. [I; R1 = H, alkyl; R2 = heteroaryl, heterocyclyl, aryl fused to heteroaryl or heterocyclyl; L = haloalkyl, alkyl, aryl, etc.; Y1-Y3 = H, halo, alkyl, etc.; Z = N, CH], phosphodiesterase 7 (PDE 7) inhibitors useful in treating T-cell mediated diseases, were prepared Thus, reacting 2,4-dichloro-6,7-dimethoxyquinazoline with 4-methylsulfonylbenzylamine.HCl followed by palladium-catalyzed coupling of the intermediate with Et 2-amino-4-methylthiazole-5-carboxylate afforded II.

IT **479072-12-3P 479072-13-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline and pyrido[2,3-d]pyrimidine inhibitors of phosphodiesterase (PDE) 7)

RN 479072-12-3 HCAPLUS

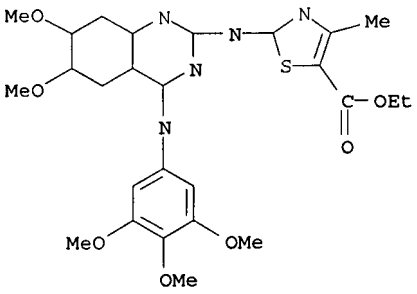
CN 5-Thiazolecarboxylic acid, 2-[[4-[(3,4-dimethoxyphenyl)amino]-6,7-dimethoxy-2-quinazolinyl]amino]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 479072-13-4 HCAPLUS

CN 5-Thiazolecarboxylic acid, 2-[[6,7-dimethoxy-4-[(3,4,5-trimethoxyphenyl)amino]-2-quinazolinyl]amino]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

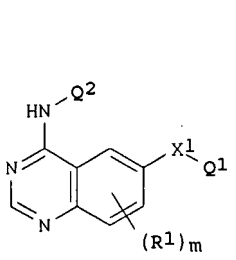


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L29 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:568090 HCAPLUS
DN 127:248122
TI Quinazoline derivatives as antitumor agents
IN Barker, Andrew John; Johnstone, Craig
PA Zeneca Limited, UK
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO---9730034	A1	19970821	1997WO-GB00344	19970210 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA---2242102	A1	19970821	1997CA-2242102	19970210 <--
	CA---2242102	C	20060822		
	AU---9716126	A	19970902	1997AU-0016126	19970210 <--
	AU----707339	B2	19990708		
	EP----880507	A1	19981202	1997EP-0902496	19970210 <--
	EP----880507	B1	20050413		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN---1211240	A	19990317	1997CN-0192242	19970210 <--
	JP2000504713	T	20000418	1997JP-0529073	19970210 <--
	NZ----330816	A	20000526	1997NZ-0330816	19970210 <--
	IL----125685	A	20021110	1997IL-0125685	19970210 <--
	AT----293103	T	20050415	1997AT-0902496	19970210 <--
	PT----880507	T	20050729	1997PT-0902496	19970210 <--
	ES---2239351	T3	20050916	1997ES-0902496	19970210 <--
	ZA---9701231	A	19970814	1997ZA-0001231	19970213 <--
	US---5866572	A	19990202	1997US-0796483	19970213 <--
	IN1997DE00354	A	20050311	1997IN-DE00354	19970213 <--
	NO---9803707	A	19981013	1998NO-0003707	19980813 <--
	NO----311936	B1	20020218		
	US---6399602	B1	20020604	1998US-0152070	19980911 <--
	US2003018029	A1	20030123	2002US-0136276	20020502 <--
	US---6897214	B2	20050524		
PRAI	1996GB-0003095	A	19960214 <--		
	1997WO-GB00344	W	19970210 <--		
	1997US-0796483	A3	19970213 <--		
	1998US-0152070	A1	19980911 <--		

OS MARPAT 127:248122
GI



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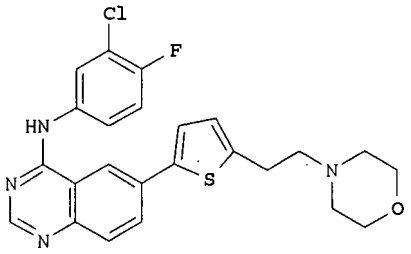


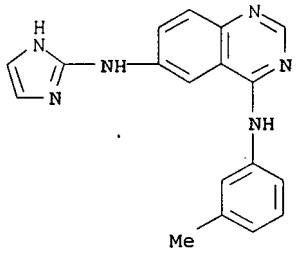
II

AB The invention concerns quinazoline derivs. I [X1 = bond, CO, C(R2)2, CH(OR2), S, C.tplbond.C, O, S, etc.; Q1 = Ph, naphthyl, or 5- or 6-membered heteroaryl optionally bearing 1-3 substituents; m = 1 or 2; R1 = H, halo, CF3, OH, NH2, cyano, etc.; R2 = H, alkyl; Q2 = Ph or 9- or 10-membered bicyclic heterocycle optionally bearing 1-3 substituents] and their pharmaceutically acceptable salts. Also disclosed are processes for preparation of I and salts, pharmaceutical compns. containing them, and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative diseases such as cancer. Examples include syntheses of 40 compds. and various intermediates. For instance, Pd(PPh3)4-catalyzed coupling of 6-bromo-4-(3-chloro-4-fluoroanilino)quinazoline-HCl with di-iso-Pr [5-(2-morpholinoethyl)thien-2-yl]boronate (prepns. given) gave 27% title compound II. At 50 mg/kg/day in athymic nude mice with human vulval epidermoid carcinoma xenografts (cell line A-431), II gave 64% inhibition of tumor volume (vs. control) after 13 days.

IT **195457-26-2P**, 6-(2-Imidazolylamino)-4-(3-methylanilino)quinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)

RN 195457-26-2 HCAPLUS

CN 4,6-Quinazolinediamine, N6-1H-imidazol-2-yl-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L29 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 1953:12395 HCAPLUS

DN 47:12395

OREF 47:2217e-f

TI 10-(2-Dialkylaminoethyl)phenothiazine

IN Nishijo, Shigeya; Nishimura, Aki

PA Nippon Chemical Industries Co.

DT Patent

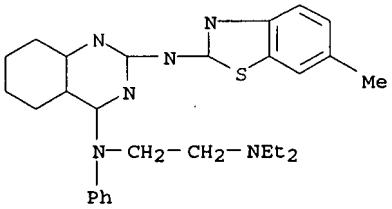
LA Unavailable

FAN.CNT 1

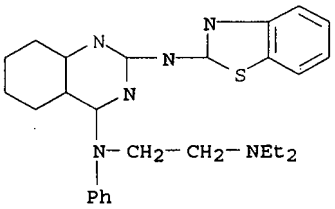
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP--25001134	B4	19500331	JP	<--

AB Phenothiazine (65 g.) in 700 mL. C6H6 refluxed 4 h. with 50 g. NaNH2, 70 g. Me2N(CH2)2Cl added, the mixture refluxed 12 h., cooled, filtered, the filtrate shaken with HCl, the aqueous layer made alkaline with NaOH, extracted with ether, and the extract distilled yielded 78 g. 10-(2-dimethylaminoethyl)phenothiazine, b1.5 190-7° (HCl salt, columns, m. 225°); 10-(2-diethylaminoethyl) analog, b1.5 195-7° (HCl salt, m. 186°).

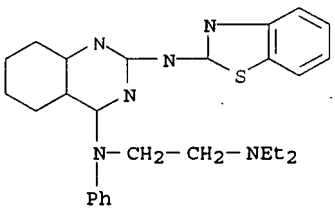
IT **873407-61-5P**, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- **873407-64-8P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- **879676-37-6P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride
RL: PREP (Preparation)
(preparation of)
RN 873407-61-5 HCAPLUS
CN Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 873407-64-8 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L29 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1953:12394 HCAPLUS
DN 47:12394
OREF 47:2217e
TI 2,4-Disubstituted amino quinazolines
IN Isler, Hans; Hueni, Albrecht
PA Ciba Pharmaceutical Products, Inc.
DT Patent
LA Unavailable
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

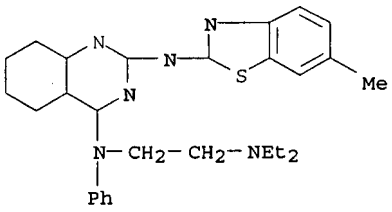
PI	US---2623878	19521230	1949US-0073435	19490128 <--

AB See Brit. 664,262 (C.A. 47, 617b).

IT **873407-61-5P**, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- **873407-64-8P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- **874497-43-5P**, Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)- **878778-78-0P**, Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)-, hydrochloride **879676-37-6P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride
RL: PREP (Preparation)
(preparation of)

RN 873407-61-5 HCAPLUS

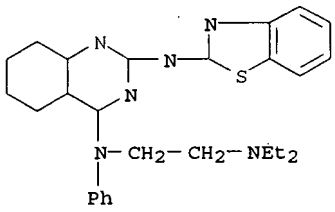
CN Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 873407-64-8 HCAPLUS

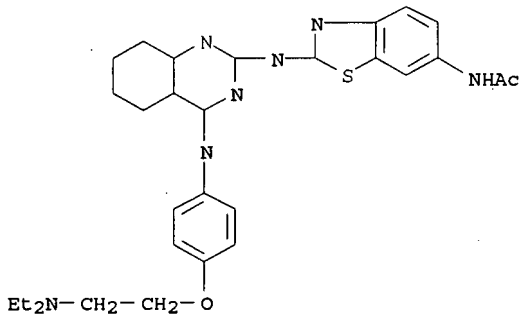
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 874497-43-5 HCAPLUS

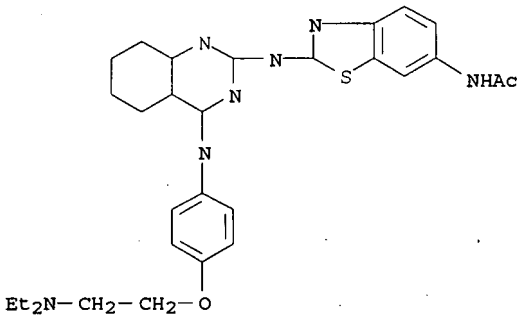
CN Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

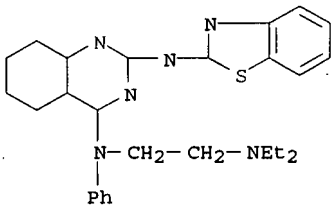
RN 878778-78-0 HCAPLUS

CN Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)-, hydrochloride (5CI) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride (5CI) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

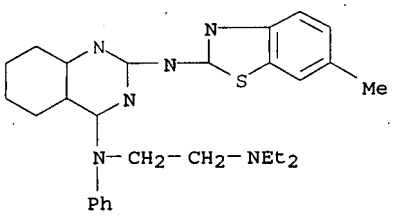
L29 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1953:12393 HCAPLUS
DN 47:12393
OREF 47:2217c-e
TI Vitamin B6 derivatives
IN Heyl, Dorothea
PA Merck & Co., Inc.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US---2583774		19520129	1948US-0024412	19480430 <--

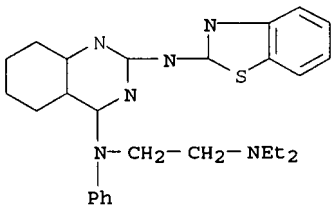
AB The acetoxime of 3-acetoxy-5-acetoxymethyl-4-formyl-2-methylpyridine (I), m. 114.5-15°, refluxed 2 h. with Ac2O, gives the 4-cyano analog (II) of I, m. 63-4°. II, refluxed 2 h. in EtOH containing 0.1% Na, gives the 3-HO analog (III) of II, m. 209-10°. III with 3 N KOH gives 4-carboxy-3-hydroxy-5-hydroxymethyl-2-methylpyridine (IV), m. 253-4° (decomposition). IV, refluxed with EtOH containing anhydrous HCl, gives the lactone of IV, m. 273-3.5° (decomposition). Alternatively, 5-chloromethyl-4-cyano-3-hydroxy-2-methylpyridine, m. 167-8° (decomposition), is hydrolyzed to 4-carbamyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine-HCl, m. 210-11° (decomposition), which in turn gives IV. The lactone has growth-promoting and antianemia activity. Cf. C.A. 44, 10740c.

IT **873407-61-5P**, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- **873407-64-8P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- **879676-37-6P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride

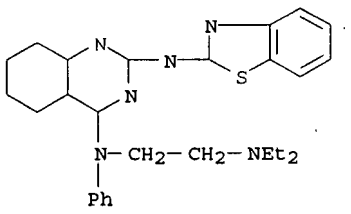
RL: PREP (Preparation)
(preparation of)
RN 873407-61-5 HCAPLUS
CN Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 873407-64-8 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-(5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride (5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L29 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1953:3470 HCAPLUS
DN 47:3470
OREF 47:617b-h
TI Heterocyclically substituted diaminoquinazolines
PA C I B A Ltd.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB----664262		19520102	1949GB-0003339	19490207 <--

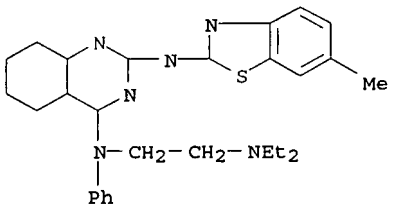
AB 2,4-Diaminoquinazolines substituted by a thiazolyl or imidazolyl group on one of the NH2 groups and by a dialkylaminoalkyl group on the other, prepared by standard methods, are useful as medicinals, some being antituberculars. 2-(Substituted amino)-4-(2-diethylaminoethylamino)quinaz

olines (substituent on the 2-NH2 given): 2-thiazolyl, m. 142-3° (HCl salt, m. 297-8°); 4-phenyl-2-thiazolyl, m. 172-4°; 4-p-tolyl-2-thiazolyl, m. 181-3°; 4,5-diphenyl-2-thiazolyl, m. 198-202° (dimethanesulfonate, m. 290-2°); 2-benzothiazolyl, m. 216-18° (HCl salt, m. 305-7°); 4-methyl-2-benzothiazolyl, m. 193-5°; 6-methyl-2-benzothiazolyl, m. 189-91° (HCl salt, m. 296-8°); 4,7-dimethyl-2-benzothiazolyl, m. 205-7° (HCl salt, m. 339-42°); 6-methoxy-2-benzothiazolyl, m. 186-7° (HCl salt, m. 293-5°); 6-butoxy-2-benzothiazolyl, m. 168-9° (HCl salt, m. 273-5°); 6-cyano-2-benzothiazolyl, m. 289-92° (HCl salt, m. 305-7°; dimethanesulfonate, m. 299-300°); 6-acetamido-2-benzothiazolyl, m. 252-7° (HCl salt, m. 317-19°); 6-nitro-2-benzothiazolyl, m. 304-6°; 6-chloro-2-benzothiazolyl, m. 210-11° (HCl salt, m. 310-11°; dimethanesulfonate, m. 302-4°); 6,7-benzo-2-benzothiazolyl, m. 220-2°; 2-benzimidazolyl, m. 224-5°; 6-methyl-2-benzimidazolyl, m. 225-7°. 2-(Substituted amino)-6-chloro-4-(2-diethylaminoethylamino)quinazolines: 2-thiazolyl, m. 180.5-1° (HCl salt, m. 286-8°); 6-methyl-2-benzothiazolyl, m. 226-8°; 6-methoxy-2-benzothiazolyl, m. 197-8° (HCl salt, m. 299-300°); 2-benzimidazolyl, m. 196-7°. Other quinazolines: 2-(6-methyl-2-benzothiazolylamino)-4-(3-diethylaminopropylamino), m. 202-4°; 2-[4-(p-bromophenyl)-2-thiazolylamino]-4-(3-diethylamino-1-methylpropylamino), m. 219-21° (HCl salt, m. 312-14°); 2-(6-methyl-2-benzothiazolylamino)-4-(3-diethylamino-1-methylpropylamino), m. 142-3° (HCl salt, m. 295-6°); 2-(2-diethylaminoethylamino)-4-(6-methyl-2-benzothiazolylamino), m. 239-41°; 2-(6-methyl-2-benzothiazolylamino)-4-[2-(1-piperidyl)ethylamino], m. 204-6° (HCl salt, m. 343-4°; dimethanesulfonate, m. 312-13°); 2-(6-acetamido-2-benzothiazolylamino)-4-[p-(2-diethylaminoethoxy)anilino], m. 166-70° (HCl salt, m. 292-7°); 2-(2-benzothiazolylamino)-4-[phenyl(2-diethylaminoethyl)amino], m. 168-9° (HCl salt, m. 278-80°); 2-(6-methyl-2-benzothiazolylamino)-4-[phenyl(2-diethylaminoethyl)amino], m. 180-2°; 2-(6-methyl-2-benzothiazolylamino)-4-[2-(2-diethylaminoethylthio)ethylamino], m. 191-3°. Intermediate 2-chloroquinazoline HCl salts: 4-[phenyl(2-diethylaminoethyl)amino], m. 239-41°; 4-[p-(2-diethylaminoethoxy)anilino], m. 211-13°; 4-(3-diethylamino-1-methylpropylamino), m. 165-7°; 4-[2-(2-diethylaminoethylthio)ethylamino], m. 102-4° (free base). Intermediate 4-hydroxyquinazolines: 2-(2-diethylaminoethylamino)-HCl, m. 201-3°; 2-(6-methyl-2-benzothiazolylamino), m. above 320°. 2-Amino-4,7-dimethylbenzothiazole, m. 158-60°. Most of the HCl salts melt with decomposition

IT **873407-61-5P**, Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- **873407-64-8P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]- **874497-43-5P**, Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)- **878778-78-0P**, Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-p-phenetidino)-, hydrochloride **879676-37-6P**, Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-, hydrochloride
RL: PREP (Preparation)
(preparation of)

RN 873407-61-5 HCAPLUS

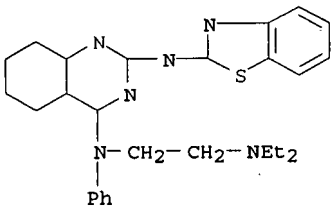
CN Quinazoline, 4-[N-(2-diethylaminoethyl)anilino]-2-(6-methyl-2-benzothiazolylamino)- (5CI) (CA INDEX NAME)



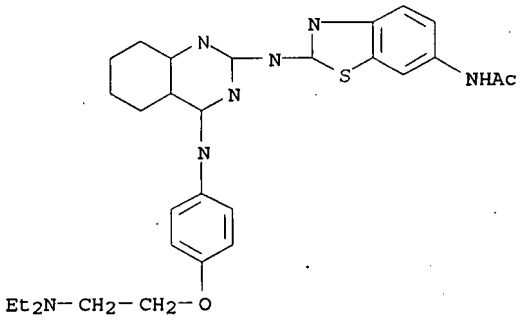
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 873407-64-8 HCAPLUS

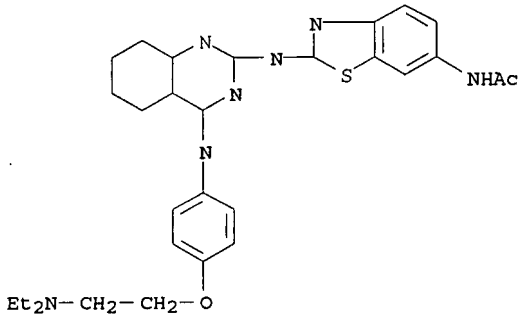
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-
(5CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 874497-43-5 HCAPLUS
CN Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-
p-phenetidino)- (5CI) (CA INDEX NAME)

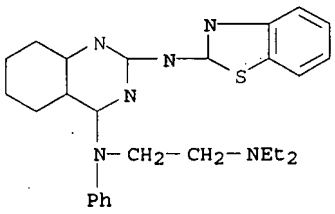


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 878778-78-0 HCAPLUS
CN Quinazoline, 2-(6-acetamido-2-benzothiazolylamino)-4-(β-diethylamino-
p-phenetidino)-, hydrochloride (5CI) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 879676-37-6 HCAPLUS
CN Quinazoline, 2-(2-benzothiazolylamino)-4-[N-(2-diethylaminoethyl)anilino]-
, hydrochloride (5CI) (CA INDEX NAME)



● HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

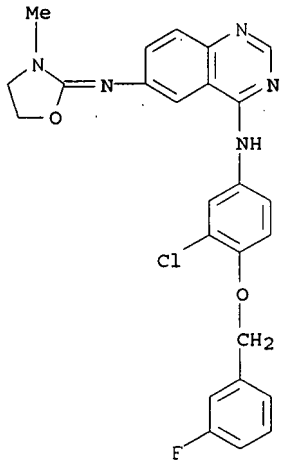
=> b uspatall
FILE 'USPATFULL' ENTERED AT 17:51:56 ON 15 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 17:51:56 ON 15 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitrn fhitstr l36 tot

L36 ANSWER 1 OF 2 USPATFULL on STN
AN 2005:118342 USPATFULL
TI Quinazoline analogs as receptor tyrosine kinase inhibitors
IN Wallace, Eli, Lyons, CO, UNITED STATES
Topalov, George, Superior, CO, UNITED STATES
Lyssikatos, Joseph, Superior, CO, UNITED STATES
Buckmelter, Alexandre, Superior, CO, UNITED STATES
Zhao, Qian, Superior, CO, UNITED STATES
PI US-20050101616 A1 20050512 <--
AI 2003US-000642440 A1 20030814 (10) <--
DT Utility
FS APPLICATION
LREP HOGAN & HARTSON LLP, ONE TABOR CENTER, SUITE 1500, 1200 SEVENTEENTH ST, DENVER, CO, 80202, US
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 1821
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention concerns quinazoline analogs of Formula I: ##STR1## where an A group is bonded to at least one of the carbons at the 5, 6, 7 or 8 position of the bicyclic ring, and the ring is substituted by up to three independent R.sup.3 groups. The invention also includes methods of using these compounds as type I receptor tyrosine kinase inhibitors and for the treatment of hyperproliferative diseases such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **851545-54-5P 851545-55-6P 851545-56-7P**
851545-57-8P 851545-58-9P 851545-59-0P
851545-60-3P 851545-61-4P 851545-62-5P
851545-63-6P 851545-64-7P 851545-65-8P
851545-66-9P 851545-67-0P 851545-68-1P
851545-69-2P 851545-70-5P
(preparation of quinazoline analogs as type I receptor tyrosine kinase inhibitors for treating hyperproliferative diseases such as cancer)
IT **851545-54-5P**
(preparation of quinazoline analogs as type I receptor tyrosine kinase inhibitors for treating hyperproliferative diseases such as cancer)
RN 851545-54-5 USPATFULL
CN 4,6-Quinazolinediamine, N4-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-N6-(3-methyl-2-oxazolidinylidene)- (9CI) (CA INDEX NAME)



L36 ANSWER 2 OF 2 USPATFULL on STN
AN 2005:50534 USPATFULL
TI Quinazoline analogs as receptor **tyrosine kinase inhibitors**
IN Wallace, Eli, Lyons, CO, UNITED STATES
Topalov, George, Superior, CO, UNITED STATES
Lyssikatos, Joseph, Superior, CO, UNITED STATES
Buckmelter, Alexandre, Superior, CO, UNITED STATES
Zhao, Qian, Superior, CO, UNITED STATES
PI US-20050043334 A1 20050224
AI 2004US-000914974 A1 20040810 (10)
RLI Continuation-in-part of Ser. No. 2003US-000642440, filed on 14 Aug 2003, PENDING
PRAI 2004US-000551718P 20040310 (60)
DT Utility
FS APPLICATION
LREP HOGAN & HARTSON LLP, ONE TABOR CENTER, SUITE 1500, 1200 SEVENTEENTH ST, DENVER, CO, 80202
CLMN Number of Claims: 106
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 2445
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides quinazoline analogs of Formula I: ##STR1##

where A is bonded to at least one of the carbons at the 5, 6, 7 or 8 position of the bicyclic ring, and the ring is substituted by up to two independent R.sup.3 groups. The invention also includes methods of using compounds of Formula I as type I receptor tyrosine kinase inhibitors and for the treatment of hyperproliferative diseases such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **845271-76-3P**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845271-77-4P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845271-79-6P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(3-oxa-1,8-diazaspiro[4.5]dec-1-en-2-yl)amino]quinazoline
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)
IT **845271-69-4P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-72-9P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845271-74-1P**, 4-[[3-Chloro-4-(3-fluorobenzyloxy)phenyl]amino]-6-[(3,8-dioxa-1-azaspiro[4.5]dec-1-en-2-yl)amino]quinazoline **845271-75-2P**, 6-[(3,8-Dioxa-1-azaspiro[4.5]dec-1-en-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-78-5P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-

6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazol-5-yl]ethanone **845271-81-0P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3-oxa-1,8-diazaspiro[4.5]dec-1-en-8-yl]ethanone **845271-82-1P**, 6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-83-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(1-oxa-3,8-diazaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-85-4P**, 1-[2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-en-8-yl]ethanone **845271-87-6P**, [4-Methyl-2-[[4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]methanol **845271-88-7P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-89-8P**, 6-[(1,8-Dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-90-1P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-91-2P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-92-3P**, 6-[(5,5-Dimethyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845271-93-4P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-94-5P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-95-6P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845271-96-7P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845271-97-8P**, 4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845271-98-9P**, rel-(1R)-1-[(5S)-5-Methyl-2-[[4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-5-yl]ethanol **845271-99-0P**, 6-[(4,5-Dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-00-6P**, [2-[[4-((3-Chloro-4-((pyridin-2-yl)methoxy)phenyl)amino)quinazolin-6-yl]amino]-4-methyl-4,5-dihydrooxazol-4-yl]methanol **845272-01-7P**, rel-(1R)-1-[(5S)-2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-5-methyl-4,5-dihydrooxazol-5-yl]ethanol **845272-02-8P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,4-dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-03-9P**, rel-(1R)-1-[(5S)-2-[[4-[[4-[(3-Fluorobenzyl)oxy]-3-chlorophenyl]amino]quinazolin-6-yl]amino]-5-methyl-4,5-dihydrooxazol-5-yl]ethanol **845272-04-0P**, 6-[(5-Methyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-05-1P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-06-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(1,8-dioxa-3-azaspiro[4.5]dec-2-en-2-yl)amino]quinazoline **845272-07-3P**, 6-[(4-Methyl-4,5-dihydrooxazol-2-yl)amino]-4-[[3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazoline **845272-08-4P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845272-09-5P**, 4-[[3-Methyl-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(3a,4,6,6a-tetrahydrofuro[3,4-d]oxazol-2-yl)amino]quinazoline **845272-10-8P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-11-9P**, 4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-12-0P**, 4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845272-14-2P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]oxazol-2-yl)amino]quinazoline **845272-16-4P**, [2-[[4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]quinazolin-6-yl]amino]-4-methyl-4,5-dihydrooxazol-4-yl]methanol **845272-17-5P**, 4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(6-oxa-4-azaspiro[2.4]hept-4-en-5-yl)amino]quinazoline **845272-18-6P**, [2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-4-hydroxymethyl-4,5-dihydrooxazol-4-yl]methanol **845272-19-7P**, (1R)-1-[(4S)-2-[[4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quina

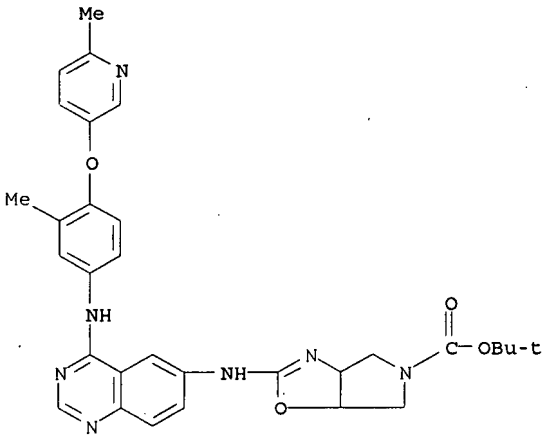
zolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]ethanol **845272-21-1P**,
(R)-4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-22-2P**,
(S)-4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]-6-[(4-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-23-3P**,
(S)-4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-24-4P**,
(R)-4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-6-[(5-methyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-25-5P**,
4-[[4-[(5-Chloropyridin-3-yl)oxy]-3-methylphenyl]amino]-6-[(4,4-dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-26-6P**,
4-[[3-Methyl-4-[(pyridin-3-yl)oxy]phenyl]amino]-6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-27-7P**,
4-[[4-[(5-Fluoropyridin-3-yl)oxy]-3-methylphenyl]amino]-6-[(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)amino]quinazoline **845272-30-2P**,
4-[[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]amino]-6-[(4,5-dihydrooxazol-2-yl)(methyl)amino]quinazoline **845272-32-4P**, [2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-4,5-dihydrooxazol-4-yl]methanol
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

IT **845271-80-9**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3-oxa-1,8-diazaspiro[4.5]dec-1-ene-8-carboxylic acid tert-butyl ester **845271-84-3**, 2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-ene-8-carboxylic acid tert-butyl ester **845271-86-5**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-1-oxa-3,8-diazaspiro[4.5]dec-2-ene-8-carboxylic acid tert-butyl ester **845272-13-1**, 2-[[4-[[3-Chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845272-15-3**, 2-[[4-[[3-Chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester **845272-20-0**, 6-[[(4S)-4-((1R)-1-(tert-Butoxy)ethyl)-4,5-dihydrooxazol-2-yl]amino]-4-[[3-chloro-4-[(thiazol-2-yl)methoxy]phenyl]amino]quinazoline
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

IT **845271-76-3P**, 2-[[4-[[3-Methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl]amino]quinazolin-6-yl]amino]-3a,4,6,6a-tetrahydropyrrolo[3,4-d]oxazole-5-carboxylic acid tert-butyl ester
(preparation of aminoquinazolines as receptor tyrosine kinase inhibitors)

RN 845271-76-3 USPATFULL

CN 5H-Pyrrolo[3,4-d]oxazole-5-carboxylic acid, 3a,4,6,6a-tetrahydro-2-[[4-[[3-methyl-4-[(6-methyl-3-pyridinyl)oxy]phenyl]amino]-6-quinazolinyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



=> d bib abs hitstr l35 tot

L35 ANSWER 1 OF 9 USPATFULL on STN
AN 2005:203316 USPATFULL

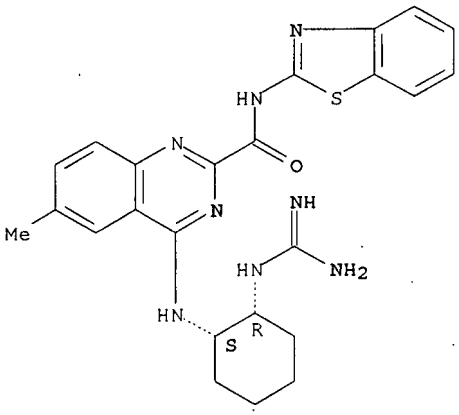
TI Quinazoline derivative and medicine
IN Okano, Masahiko, Kyoto, JAPAN
Oyama, Tatsuya, Kyoto, JAPAN
PI US-20050176741 A1 20050811
AI 2003US-000512954 A1 20030428 (10)
2003WO-JP0005432 20030428
PRAI 2002JP-000125452 20020426
2003JP-2002272314 20020918
2003JP-2002373400 20021225
DT Utility
FS APPLICATION
LREP DARBY & DARBY P.C., P. O. BOX 5257, NEW YORK, NY, 10150-5257, US
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3413
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An object of the present invention is to provide an antipruritic agent having a novel action mechanism. The present invention provides an antipruritic agent comprising a compound represented by the following general formula (1): ##STR1## wherein R.sup.1 represents a hydrogen atom or alkyl; the ring Q represents a cyclohexylene group or a phenylene group; A.sup.1 and A.sup.2 represent a single bond or an alkylene group; E represents --NHCO--; A.sup.3 represents a single bond or a divalent saturated or unsaturated aliphatic hydrocarbon group; R.sup.3 represents a non-cyclic aliphatic hydrocarbon group; and R.sup.4 and R.sup.5 are the same or different and each represents a hydrogen atom or alkyl, or a pharmaceutically acceptable salt thereof as an active ingredient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **620953-35-7P 620953-79-9P 620955-73-9P**
620955-97-7P 620956-60-7P
(preparation of quinazoline derivs. as antipruritic agents)
RN 620953-35-7 USPATFULL
CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-N-2-benzothiazolyl-6-methyl-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

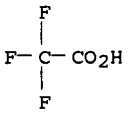
CRN 620953-34-6
CMF C24 H26 N8 O S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

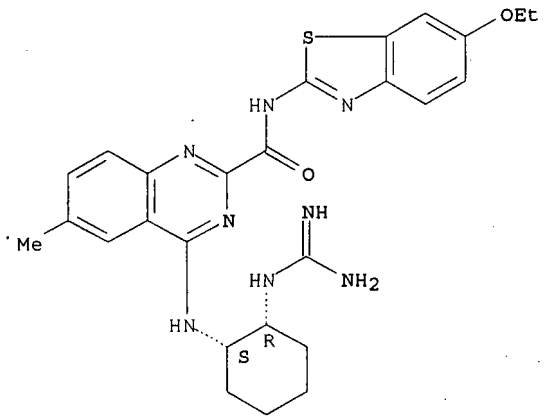


RN 620953-79-9 USPATFULL
CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-N-(6-ethoxy-2-benzothiazolyl)-6-methyl-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

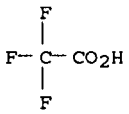
CRN 620953-78-8
CMF C26 H30 N8 O2 S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

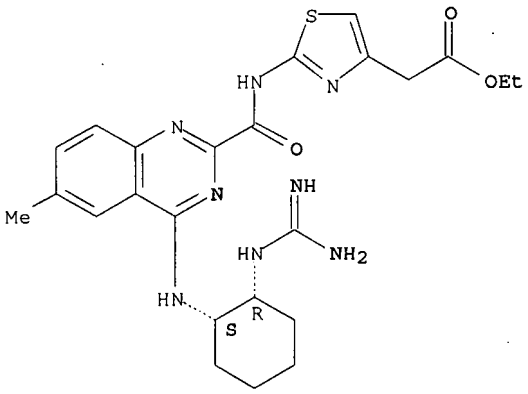


RN 620955-73-9 USPATFULL
CN 4-Thiazoleacetic acid, 2-[[[4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-2-quinazolinyl]carbonyl]amino]-, ethyl ester, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

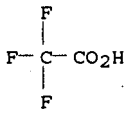
CRN 620955-72-8
CMF C24 H30 N8 O3 S

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

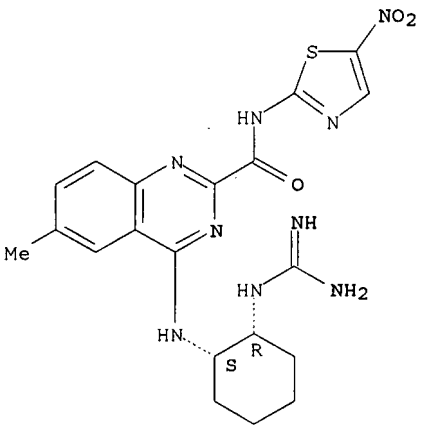


RN 620955-97-7 USPATFULL
CN 2-Quinazolinecarboxamide, 4-[[(1R,2S)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-N-(5-nitro-2-thiazolyl)-, rel-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

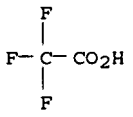
CRN 620955-96-6
CMF C20 H23 N9 O3 S

Relative stereochemistry.



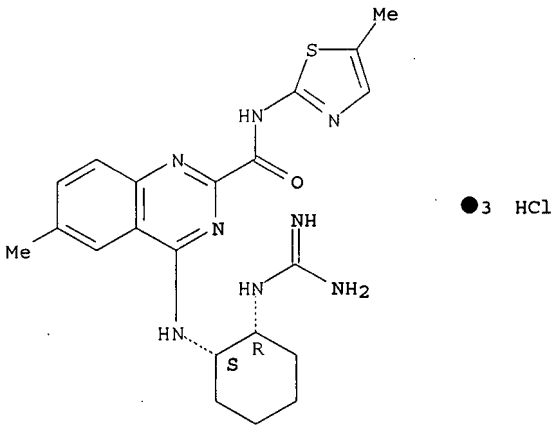
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 620956-60-7 USPATFULL
CN 2-Quinazolinecarboxamide, 4-[[(1S,2R)-2-[(aminoiminomethyl)amino]cyclohexyl]amino]-6-methyl-N-(5-methyl-2-thiazolyl)-, trihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

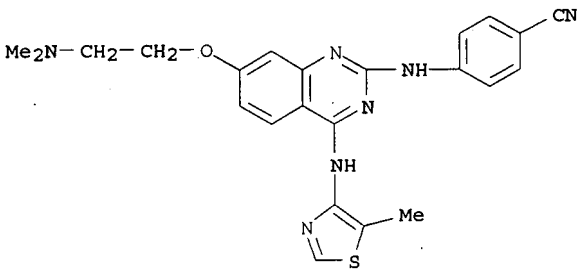


●3 HCl

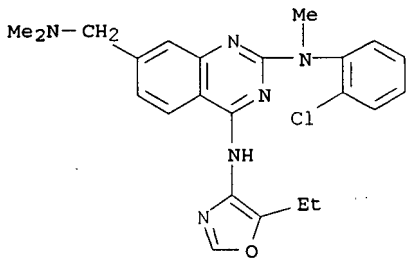
L35 ANSWER 2 OF 9 USPATFULL on STN
AN 2004:2473 USPATFULL
TI Compositions useful as inhibitors of protein kinases
IN Bebbington, David, Newbury, UNITED KINGDOM
Binch, Hayley, Harwell, UNITED KINGDOM
Charrier, Jean-Damien, Grove Wantage, UNITED KINGDOM
Everitt, Simon, Beaconsfield, UNITED KINGDOM
Golec, Julian M. C., Ashbury, UNITED KINGDOM
Kay, David, Wiltshire, UNITED KINGDOM
Knegtel, Ronald, Abingdon, UNITED KINGDOM
Miller, Andrew, Upton, UNITED KINGDOM
Pierard, Francoise, Drayton, UNITED KINGDOM
PI US-20040002496 A1 20040101
US-----7179826 B2 20070220
AI 2003US-000389709 A1 20030314 (10)
PRAI 2003WO-US0007904 20030314
2002US-000364840P 20020315 (60)
DT Utility
FS APPLICATION
LREP Michael C. Badia, Vertex Pharmaceuticals Incorporated, 130 Waverly Street, Cambridge, MA, 02139-4242
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compositions comprising said compounds and methods of using the compositions in the treatment of various disease, conditions, or disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **603932-31-6 603932-32-7**
(azolylaminoazine compds. as inhibitors of protein kinases, therapeutic use, and use with other agents)
RN 603932-31-6 USPATFULL
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-methyl-4-

thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



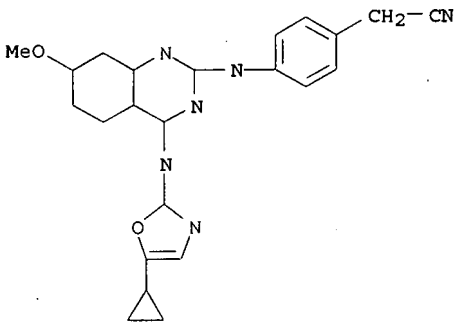
RN 603932-32-7 USPATFULL
CN 2,4-Quinazolinediamine, N2-(2-chlorophenyl)-7-[(dimethylamino)methyl]-N4-(5-ethyl-4-oxazolyl)-N2-methyl- (9CI) (CA INDEX NAME)



L35 ANSWER 3 OF 9 USPATFULL on STN
AN 2003:319324 USPATFULL
TI Compositions useful as inhibitors of protein kinases
IN Bebbington, David, Newbury, UNITED KINGDOM
Binch, Hayley, Harwell, UNITED KINGDOM
Charrier, Jean-Damien, Grove Wantage, UNITED KINGDOM
Everitt, Simon, Beaconsfield, UNITED KINGDOM
Golec, Julian M.C., Ashbury, UNITED KINGDOM
Kay, David, Purton, UNITED KINGDOM
Knegtel, Ronald, Abingdon, UNITED KINGDOM
Miller, Andrew, Upton, UNITED KINGDOM
Pierard, Francoise, Drayton, UNITED KINGDOM
Pierce, Albert C., Cambridge, MA, UNITED STATES
PI US-20030225073 A1 20031204
US-----6846928 B2 20050125
AI 2003US-000389707 A1 20030314 (10)
PRAI 2002US-000364842P 20020315 (60)
DT Utility
FS APPLICATION
LREP Michael C. Badia, Vertex Pharmaceuticals Incorporated, 130 Waverly Street, Cambridge, MA, 02139-4242
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1902
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compositions comprising said compounds and methods of using the compositions in the treatment of various disease, conditions, or disorders.

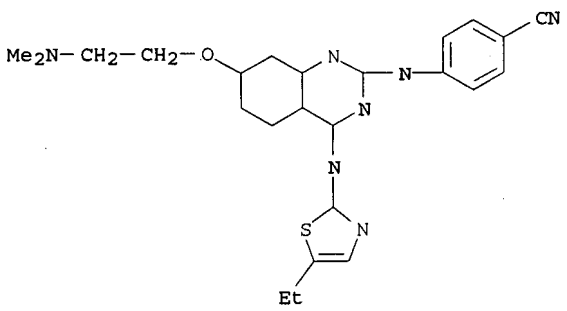
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **606092-42-6P 606092-43-7P 606092-57-3P**
(preparation of thiazolylaminopyrimidines and related compds. as inhibitors of protein kinases)
RN 606092-42-6 USPATFULL
CN Benzeneacetonitrile, 4-[[4-[(5-cyclopropyl-2-oxazolyl)amino]-7-methoxy-2-

quinazolinyl]amino]- (9CI) (CA INDEX NAME)



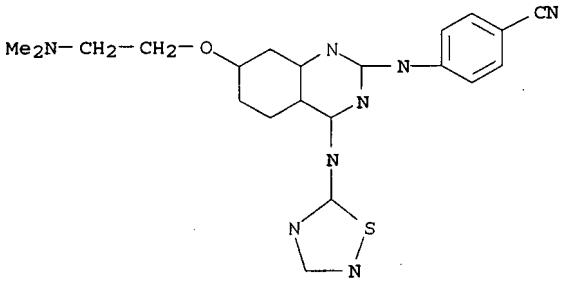
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 606092-43-7 USPATFULL
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-ethyl-2-thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 606092-57-3 USPATFULL
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-(1,2,4-thiadiazol-5-ylamino)-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L35 ANSWER 4 OF 9 USPATFULL on STN
AN 2003:24186 USPATFULL
TI Quinazoline derivatives
IN Barker, Andrew John, Cheshire, UNITED KINGDOM
Johnstone, Craig, Cheshire, UNITED KINGDOM
PA ZENECA LIMITED (non-U.S. corporation)
PI US-20030018029 A1 20030123
US-----6897214 B2 20050524
AI 2002US-000136276 A1 20020502 (10)
RLI Continuation of Ser. No. 1998US-000152070, filed on 11 Sep 1998, GRANTED, Pat. No. US-----6399602 Division of Ser. No. 1997US-000796483, filed on 13 Feb 1997, GRANTED, Pat. No. US-----5866572

PRAI 1996GB-0000003095 19960214
DT Utility
FS APPLICATION
LREP MORGAN LEWIS & BOCKIUS LLP, 1111 PENNSYLVANIA AVENUE NW, WASHINGTON, DC, 20004
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2620
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns quinazoline derivatives of the formula I
##STR1##

wherein X.sup.1 is a direct link or a group such as CO, C(R.sup.2).sub.2 and CH(OR.sup.2);

wherein Q.sup.1 is phenyl, naphthyl or a 5- or 6-membered heteroaryl moiety and Q.sup.1 optionally bears up to 3 substituents;

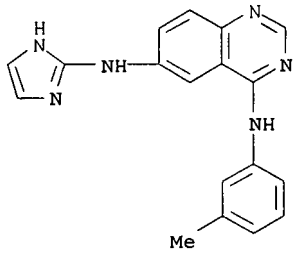
wherein m is 1 or 2 and each R.sup.1 may be a group such as hydrogen, halogeno and trifluoromethyl; and

wherein Q.sup.2 may be phenyl or a 9- or 10-membered bicyclic heterocyclic moiety and Q.sup.2 optionally bears up to 3 substituents;

or a pharmaceutically-acceptable salt thereof;

processes for their preparation, pharmaceutical compositions containing them and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative disease such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **195457-26-2P**, 6-(2-Imidazolylamino)-4-(3-methylanilino)quinazoline
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)
RN 195457-26-2 USPATFULL
CN 4,6-Quinazolinediamine, N6-1H-imidazol-2-yl-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L35 ANSWER 5 OF 9 USPATFULL on STN
AN 2002:129961 USPATFULL
TI Quinazoline derivatives
IN Barker, Andrew John, Macclesfield, UNITED KINGDOM
Johnstone, Craig, Macclesfield, UNITED KINGDOM
PA Zeneca Limited, London, UNITED KINGDOM (non-U.S. corporation)
PI US-----6399602 B1 20020604
AI 1998US-000152070 19980911 (9)
RLI Division of Ser. No. 1997US-000796483, filed on 13 Feb 1997
PRAI 1996GB-0000003095 19960214
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kifle, Bruck; Assistant Examiner: Liu, Hong
LREP Morgan, Lewis & Bockius LLP
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2935
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns quinazoline derivatives of the formula I ##STR1##

wherein X.sup.1 is a direct link or a group such as CO, C(R.sup.2).sub.2 and CH(OR.sup.2);

wherein Q.sup.1 is phenyl, naphthyl or a 5- or 6-membered heteroaryl moiety and Q.sup.1 optionally bears up to 3 substituents;

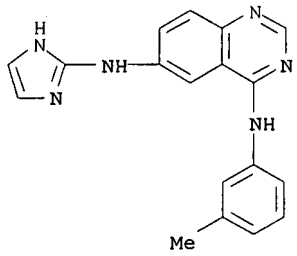
wherein m is 1 or 2 and each R.sup.1 may be a group such as hydrogen, halogeno and trifluoromethyl; and

wherein Q.sup.2 may be phenyl or a 9- or 10-membered bicyclic heterocyclic moiety and Q.sup.2 optionally bears up to 3 substituents;

or a pharmaceutically-acceptable salt thereof;

processes for their preparation, pharmaceutical compositions containing them and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative disease such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **195457-26-2P**, 6-(2-Imidazolylamino)-4-(3-methylanilino)quinazoline
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)
RN 195457-26-2 USPATFULL
CN 4,6-Quinazolinediamine, N6-1H-imidazol-2-yl-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L35 ANSWER 6 OF 9 USPATFULL on STN
AN 1999:15926 USPATFULL
TI Quinazoline derivatives
IN Barker, Andrew John, Macclesfield, United Kingdom
Johnstone, Craig, Macclesfield, United Kingdom
PA Zeneca Limited, London, United Kingdom (non-U.S. corporation)
PI US-----5866572 19990202
AI 1997US-000796483 19970213 (8)
PRAI 1996GB-0000003095 19960214
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro, LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2526
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns quinazoline derivatives of the formula I ##STR1## wherein X.sup.1 is a direct link or a group such as CO, C(R.sup.2).sub.2 and CH(OR.sup.2);

wherein Q.sup.1 is phenyl, naphthyl or a 5- or 6-membered heteroaryl moiety and Q.sup.1 optionally bears up to 3 substituents;

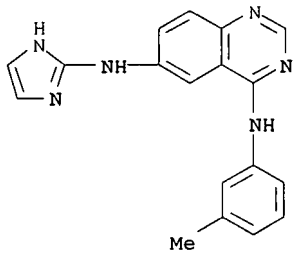
wherein m is 1 or 2 and each R.sup.1 may be a group such as hydrogen, halogeno and trifluoromethyl; and

wherein Q.sup.2 may be phenyl or a 9- or 10-membered bicyclic heterocyclic moiety and Q.sup.2 optionally bears up to 3 substituents;

or a pharmaceutically-acceptable salt thereof;

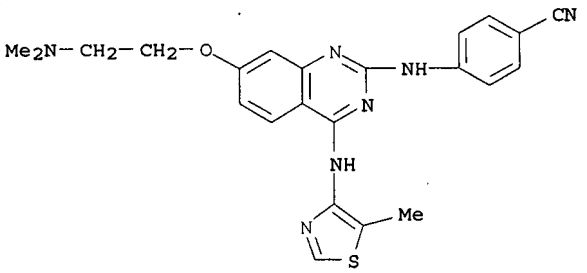
processes for their preparation, pharmaceutical compositions containing them and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative disease such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **195457-26-2P**, 6-(2-Imidazolylamino)-4-(3-methylanilino)quinazoline
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)
RN 195457-26-2 USPATFULL
CN 4,6-Quinazolinediamine, N6-1H-imidazol-2-yl-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)

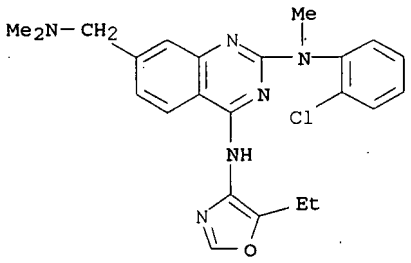


L35 ANSWER 7 OF 9 USPAT2 on STN
AN 2004:2473 USPAT2
TI Compositions useful as inhibitors of protein kinases
IN Bebbington, David, Newbury, UNITED KINGDOM
Binch, Hayley, Harwell, UNITED KINGDOM
Charrier, Jean-Damien, Grove Wantage, UNITED KINGDOM
Everitt, Simon, Bucks, UNITED KINGDOM
Golec, Julian M. C., Swindon Wilts, UNITED KINGDOM
Kay, David, Purton, UNITED KINGDOM
Knegtel, Ronald, Abingdon, UNITED KINGDOM
Miller, Andrew, Upton, UNITED KINGDOM
Pierard, Francoise, Drayton, UNITED KINGDOM
PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S. corporation)
PI US-----7179826 B2 20070220
AI 2003US-000389709 20030314 (10)
PRAI 2002US-000364840P 20020315 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Wilson, James O.; Assistant Examiner: Ward, Paul V.
LREP Vertex Pharmaceuticals Incorporated
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1641
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compositions comprising said compounds and methods of using the compositions in the treatment of various disease, conditions, or disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **603932-31-6** **603932-32-7**
(azolylaminoazine compds. as inhibitors of protein kinases, therapeutic use, and use with other agents)
RN 603932-31-6 USPAT2
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-methyl-4-thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

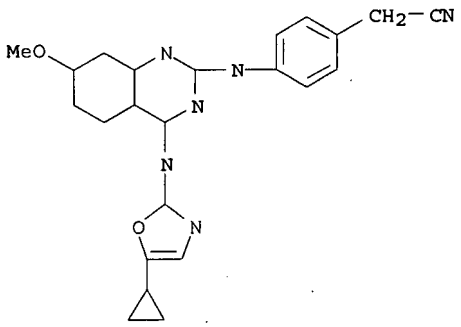


RN 603932-32-7 USPAT2
CN 2,4-Quinazolinediamine, N2-(2-chlorophenyl)-7-[(dimethylamino)methyl]-N4-(5-ethyl-4-oxazolyl)-N2-methyl- (9CI) (CA INDEX NAME)



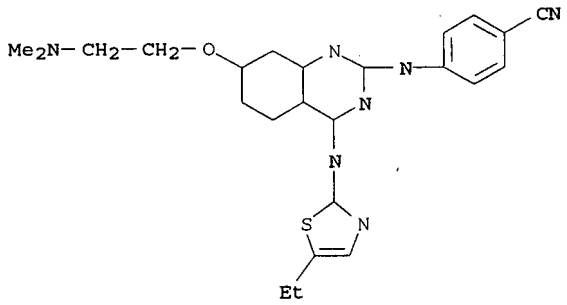
L35 ANSWER 8 OF 9 USPAT2 on STN
AN 2003:319324 USPAT2
TI Compositions useful as inhibitors of protein kinases
IN Bebbington, David, Newbury, UNITED KINGDOM
Binch, Hayley, Harwell, UNITED KINGDOM
Charrier, Jean-Damien, Grove Wantage, UNITED KINGDOM
Everitt, Simon, Beaconsfield, UNITED KINGDOM
Golec, Julian M. C., Ashbury, UNITED KINGDOM
Kay, David, Purton, UNITED KINGDOM
Knegtel, Ronald, Abingdon, UNITED KINGDOM
Miller, Andrew, Upton, UNITED KINGDOM
Pierard, Francoise, Drayton, UNITED KINGDOM
Pierce, Albert C., Cambridge, MA, United States
PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S. corporation)
PI US-----6846928 B2 20050125
AI 2003US-000389707 20030314 (10)
PRAI 2002US-000364842P 20020315 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Solola, Taofiq
LREP Badia, Michael C., Vertex Pharmaceuticals Incorporated
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compositions comprising said compounds and methods of using the compositions in the treatment of various disease, conditions, or disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **606092-42-6P 606092-43-7P 606092-57-3P**
(preparation of thiazolylaminopyrimidines and related compds. as inhibitors of protein kinases)
RN 606092-42-6 USPAT2
CN Benzeneacetonitrile, 4-[[4-[(5-cyclopropyl-2-oxazolyl)amino]-7-methoxy-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



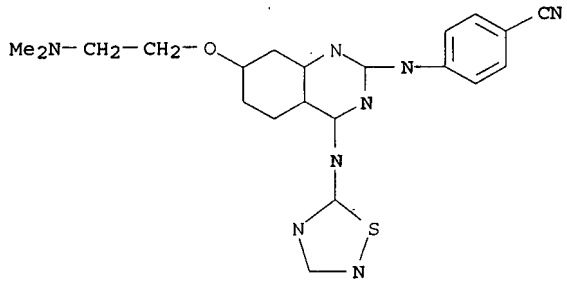
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 606092-43-7 USPAT2
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-[(5-ethyl-2-thiazolyl)amino]-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 606092-57-3 USPAT2
CN Benzonitrile, 4-[[7-[2-(dimethylamino)ethoxy]-4-(1,2,4-thiadiazol-5-ylamino)-2-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



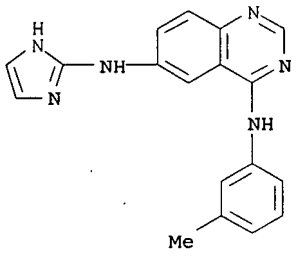
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L35 ANSWER 9 OF 9 USPAT2 on STN
AN 2003:24186 USPAT2
TI Quinazoline derivatives
IN Barker, Andrew John, Macclesfield, UNITED KINGDOM
Johnstone, Craig, Macclesfield, UNITED KINGDOM
PA Zeneca Limited, London, UNITED KINGDOM (non-U.S. corporation)
PI US-----6897214 B2 20050524
AI 2002US-000136276 20020502 (10)
RLI Continuation of Ser. No. 1998US-000152070, filed on 11 Sep 1998, Pat. No. US-----6399602 Division of Ser. No. 1997US-000796483, filed on 13 Feb 1997, Pat. No. US-----5866572
PRAI 1996GB-0000003095 19960214
DT Utility
FS GRANTED

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Liu, Hong
LREP Morgan, Lewis & Bockius LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2704
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns quinazoline derivatives of the formula I
##STR1##

wherein X.sup.1 is a direct link or a group such as CO, C(R.sup.2).sub.2 and CH(OR.sup.2);
wherein Q.sup.1 is phenyl, naphthyl or a 5- or 6-membered heteroaryl moiety and Q.sup.1 optionally bears up to 3 substituents;
wherein m is 1 or 2 and each R.sup.1 may be a group such as hydrogen, halogeno and trifluoromethyl; and
wherein Q.sup.2 may be phenyl or a 9- or 10-membered bicyclic heterocyclic moiety and Q.sup.2 optionally bears up to 3 substituents;
or a pharmaceutically-acceptable salt thereof;
processes for their preparation, pharmaceutical compositions containing them and the use of their receptor tyrosine kinase inhibitory properties in the treatment of proliferative disease such as cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **195457-26-2P**, 6-(2-Imidazolylamino)-4-(3-methylanilino)quinazoline
(preparation of quinazoline derivs. as antitumor agents and antiproliferatives)
RN 195457-26-2 USPAT2
CN 4,6-Quinazolinediamine, N6-1H-imidazol-2-yl-N4-(3-methylphenyl)- (9CI)
(CA INDEX NAME)



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FILE 'REGISTRY' ENTERED AT 17:15:33 ON 15 AUG 2007

FILE 'HCAPLUS' ENTERED AT 17:15:33 ON 15 AUG 2007
L2 TRA L1 1- RN : 171 TERMS

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L3 171 SEA L2
L4 124 L3 AND NCNC3-C6/ES
L5 STR
L6 0 L5
E BENZOPYRIMIDINE/CN
L7 STR
L8 50 L7
L9 307609 NCNC3-C6/ES
L10 113460 591.100.47/RID
SAV TEM J440C1/A L12
L11 STR L5

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L13         125 L11 FULL SUB=L10
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                E TOPALOV G/AU
L19          10 E3-5
                E LYSSIKATOS J/AU
L20          50 E4-8
                E BUCKMELTER A/AU
L21          13 E4-5
                E ZHAO Q/AU
L22         570 E3-21
                E ZHAO QIAN/AU
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L24          99 (ARRAY (L) BIOPHARMA?)/CS,PA
L25           3 L15 AND L17-24
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L30           0 L13

     FILE 'USPATFULL, USPAT2' ENTERED AT 17:48:27 ON 15 AUG 2007
L31          11 L13
L32           1 L31 AND L1
L33          10 L31 NOT L32
L34           1 L33 AND TYROSINE KINASE INHIBITORS/TI
L35           9 L33 NOT L34
L36           2 L32,L34

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L37           0 L13

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=> b casre
FILE 'CASREACT' ENTERED AT 13:25:35 ON 16 AUG 2007
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FILE CONTENT:1840 - 11 Aug 2007 VOL 147 ISS 8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

*************************************************************
*                                                           *
*     CASREACT now has more than 12 million reactions       *
*                                                           *
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Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

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L2                STR
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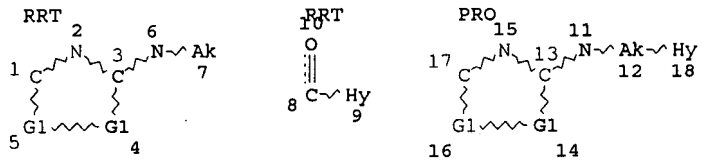


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DEFAULT ECLEVEL IS LIMITED
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ECOUNT  IS E8 C  E2 N  AT  18

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L4             3 SEA FILE=CASREACT SSS FUL L2 (    90 REACTIONS)

100.0% DONE  421708 VERIFIED      90 HIT RXNS                      3 DOCS
SEARCH TIME: 00.00.08


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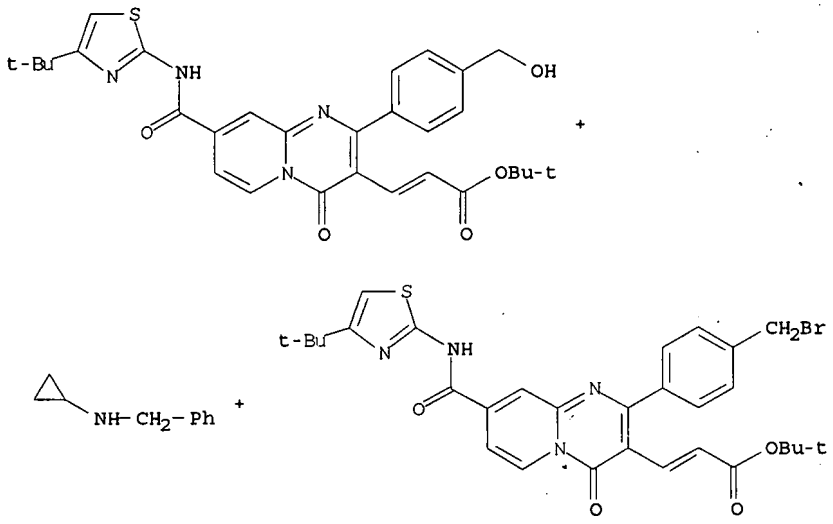
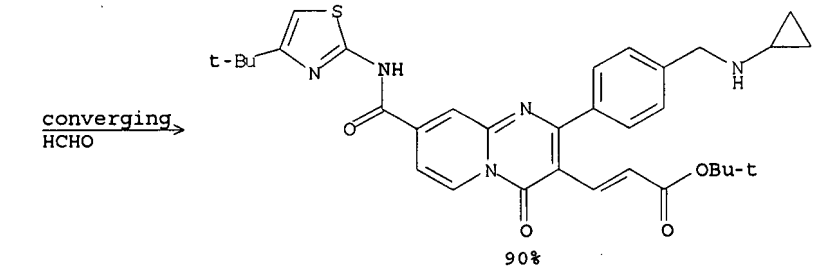
L4   ANSWER 1 OF 3  CASREACT  COPYRIGHT 2007 ACS on STN
AN   146:114213  CASREACT
TI   MexAB-OprM specific efflux pump inhibitors in Pseudomonas aeruginosa.
     Exploration of aromatic substituents
AU   Yoshida, Ken-ichi; Nakayama, Kiyoshi; Yokomizo, Yoshihiro; Ohtsuka,
     Masami; Takemura, Makoto; Hoshino, Kazuki; Kanda, Hiroko; Namba, Kenji;
     Nitanai, Hironobu; Zhang, Jason Z.; Lee, Ving J.; Watkins, William J.
CS   Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd.,
     Edogawa-ku, Tokyo, 134-8630, Japan
SO   Bioorganic & Medicinal Chemistry (2006), 14(24), 8506-8518
     CODEN: BMECEP; ISSN: 0968-0896
PB   Elsevier Ltd.
DT   Journal
LA   English
```

AB A series of 4-oxo-4H-pyrido[1,2-a]pyrimidine derivs., derivatized at the 2-position with aromatic substituents, were synthesized by the Suzuki cross-coupling method and evaluated for their ability to potentiate the activity of the fluoroquinolone levofloxacin and the antipseudomonas β-lactam aztreonam in Pseudomonas aeruginosa. By incorporating hydrophilic substituents onto the aryl nucleus, the authors found a morpholine analog that possessed improved solubility, retained activity in vitro, and displayed potentiation activity in vivo in a rat model of P. aeruginosa pneumonia.

RX(158) OF 185 - 4 STEPS



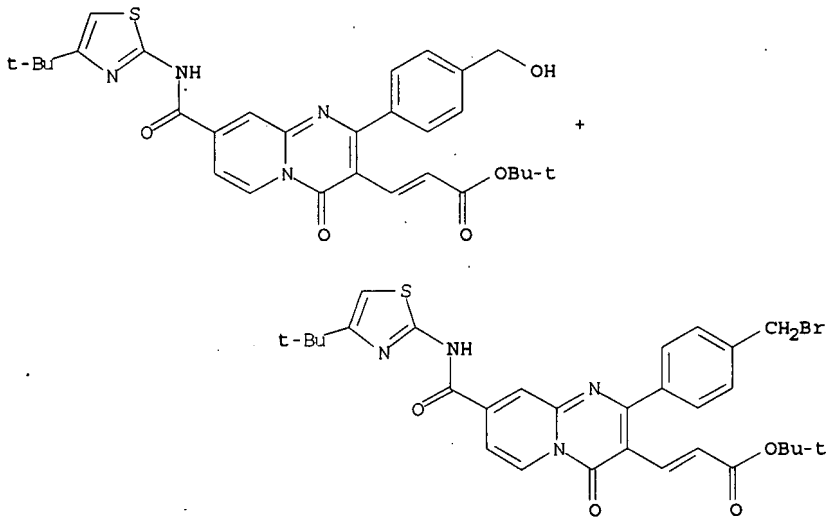
RX(158) OF 185 - 4 STEPS



90%

CON: STEP(1.1) 0 deg C
STEP(1.2) 20 minutes, 0 deg C; 19 hours, room temperature
STEP(2.1) 16 hours, room temperature, 1 atm
STEP(2.2) room temperature
STEP(3.1) 10 minutes, room temperature
STEP(3.2) 17 hours, room temperature
STEP(4) 30 minutes, 0 deg C

RX(184) OF 185 - 6 STEPS



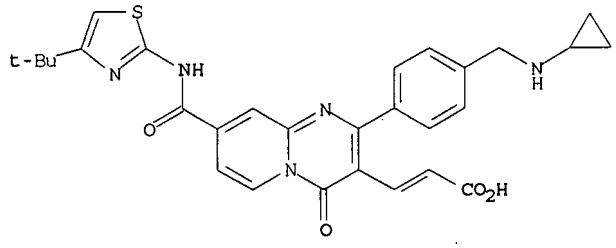
RX(184) OF 185 - 6 STEPS

converging

Cyclopropylamine,

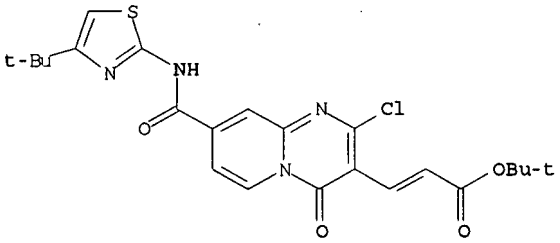
PhCH2Br

HCHO



CON: STEP(1.1) room temperature; 17 hours, room temperature
STEP(2.1) 0 deg C
STEP(2.2) 20 minutes, 0 deg C; 19 hours, room temperature
STEP(3.1) 16 hours, room temperature, 1 atm
STEP(3.2) room temperature
STEP(4.1) 10 minutes, room temperature
STEP(4.2) 17 hours, room temperature
STEP(5) 1.5 hours, room temperature
STEP(6) 30 minutes, 0 deg C

RX(185) OF 185 - 7 STEPS



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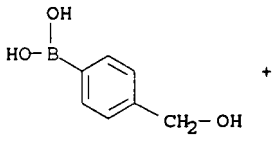

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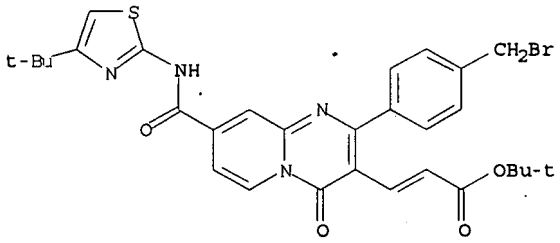
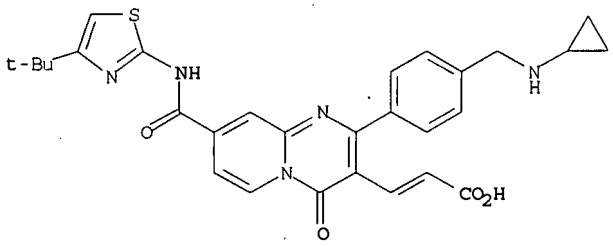
RX(185) OF 185 - 7 STEPS



converging
Cyclopropylamine,
PhCH2Br
HCHO

RX(185) OF 185 - 7 STEPS



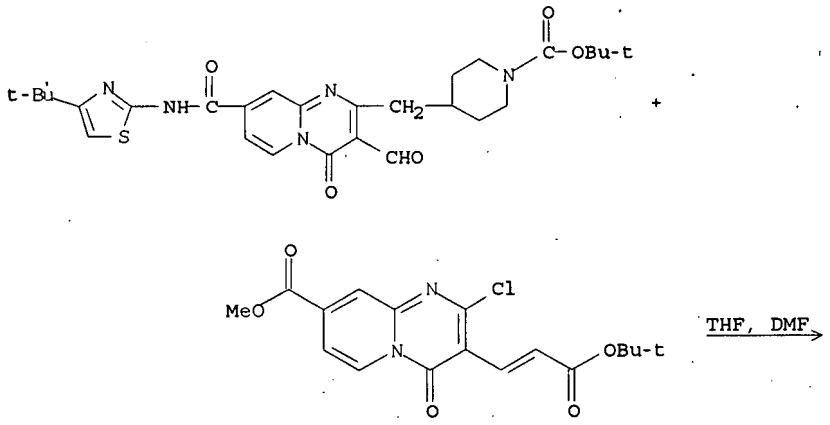
NOTE: Suzuki coupling
CON: STEP(1.1) room temperature; 17 hours, room temperature
STEP(2.1) 0 deg C
STEP(2.2) 20 minutes, 0 deg C; 19 hours, room temperature
STEP(3.1) 16 hours, room temperature, 1 atm
STEP(3.2) room temperature
STEP(4.1) 10 minutes, room temperature
STEP(4.2) 17 hours, room temperature
STEP(5) 1.5 hours, room temperature
STEP(6) reflux
STEP(7) 30 minutes, 0 deg C

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

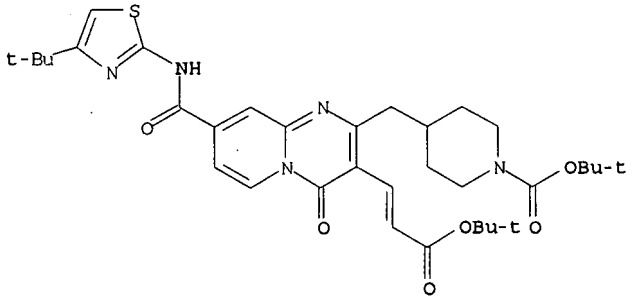
L4 ANSWER 2 OF 3 CASREACT COPYRIGHT 2007 ACS on STN

AN 144:366386 CASREACT
TI MexAB-OprM specific efflux pump inhibitors in Pseudomonas aeruginosa. Part 5: Carbon-substituted analogues at the C-2 position
AU Yoshida, Ken-ichi; Nakayama, Kiyoshi; Kuru, Noriko; Kobayashi, Shozo; Ohtsuka, Masami; Takemura, Makoto; Hoshino, Kazuki; Kanda, Hiroko; Zhang, Jason Z.; Lee, Ving J.; Watkins, William J.
CS Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd, Edogawa-ku, Tokyo, 134-8630, Japan
SO Bioorganic & Medicinal Chemistry (2006), 14(6), 1993-2004
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
AB A series of 4-oxo-4H-pyrido[1,2-a]pyrimidine derivs., derivatized at the 2-position with carbon-linked substituents, were synthesized and evaluated for their ability to potentiate the activity of the fluoroquinolone levofloxacin (LVFX) and the anti-pseudomonas β-lactam aztreonam (AZT) in Pseudomonas aeruginosa. Palladium-catalyzed cross-coupling methods were applied for the incorporation of aliphatic and aromatic substituents.

RX(36) OF 531



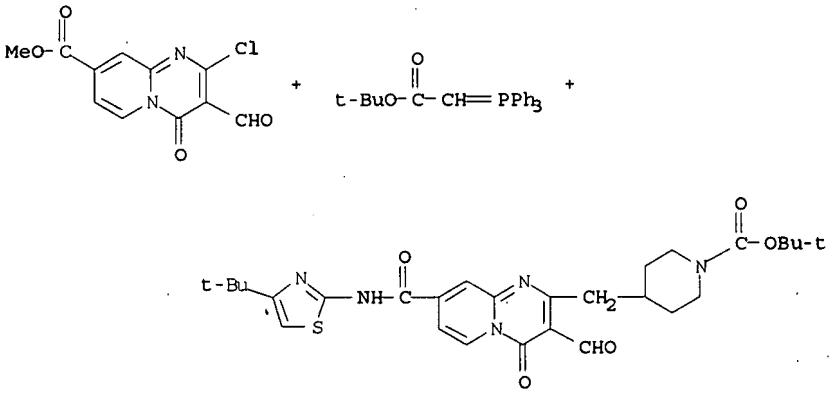
RX(36) OF 531



87%

NOTE: Wittig reaction, stereoselective
CON: 47 hours, room temperature

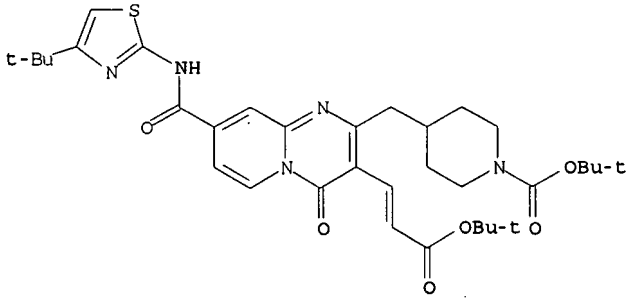
RX(56) OF 531 - 2 STEPS



(step 2)

1. THF, DMF
2. THF, DMF

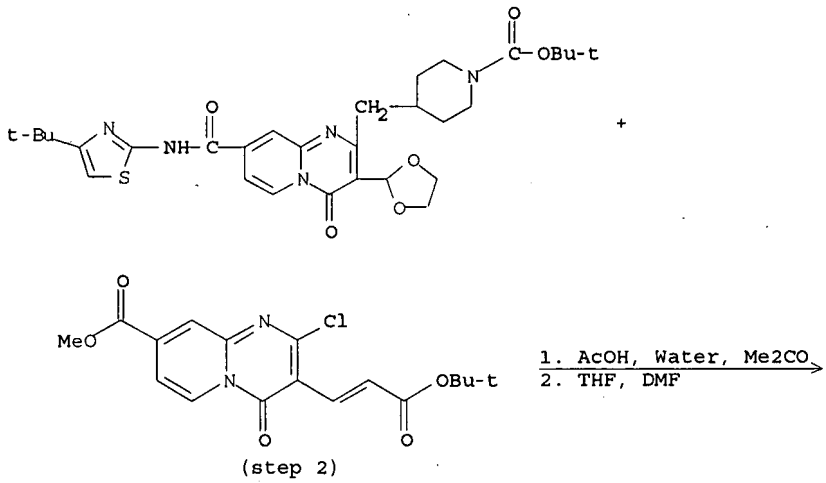
RX(56) OF 531 - 2 STEPS



87%

NOTE: 1) Wittig reaction, stereoselective, 2) Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature

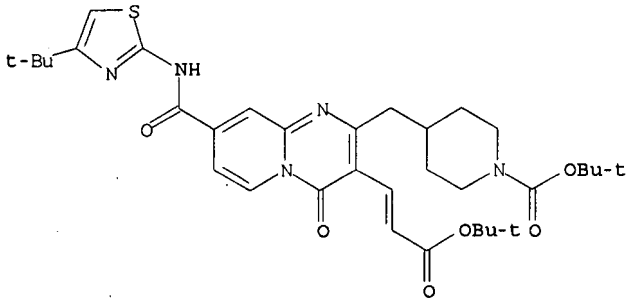
RX(84) OF 531 - 2 STEPS



(step 2)

1. AcOH, Water, Me2CO
2. THF, DMF

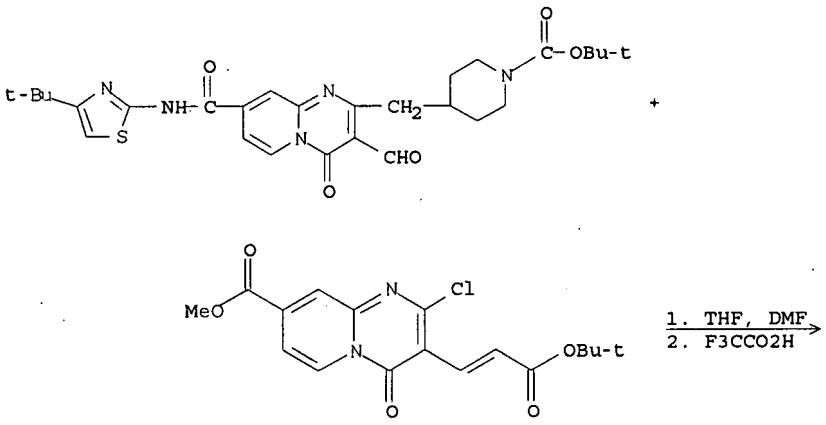
RX(84) OF 531 - 2 STEPS



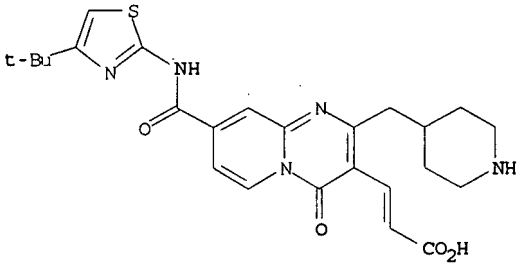
87%

NOTE: 2) Wittig reaction, stereoselective
CON: STEP(1) 1 hour, 0 deg C
STEP(2) 47 hours, room temperature

RX(85) OF 531 - 2 STEPS



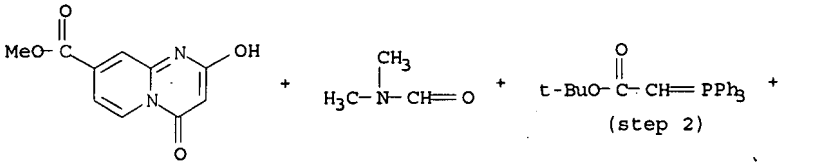
RX(85) OF 531 - 2 STEPS



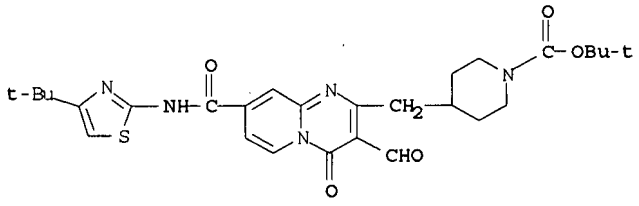
65%

NOTE: 1) Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 30 minutes, room temperature

RX(105) OF 531 - 3 STEPS



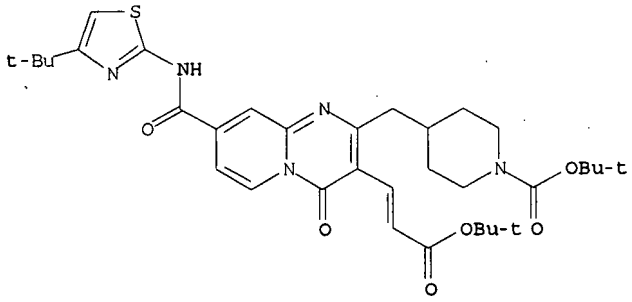
(step 2)



(step 3)

RX(105) OF 531 - 3 STEPS

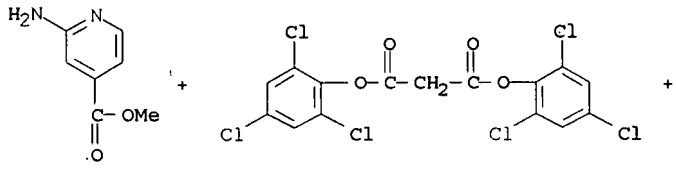
1.1. POCl3
1.2. DMF
2. THF, DMF
3. THF, DMF

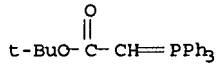


87%

NOTE: 1) Vilsmeier-Haack reaction, 2) Wittig reaction, stereoselective, 3) Wittig reaction, stereoselective
CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature

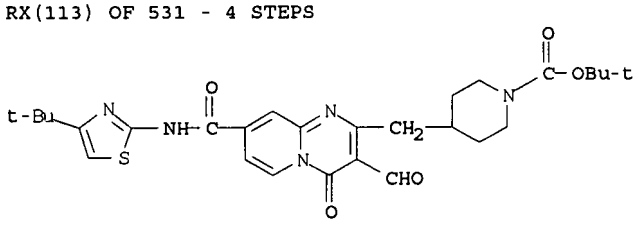
RX(113) OF 531 - 4 STEPS





(step 3)

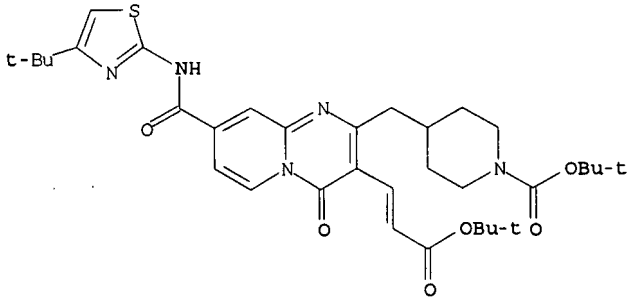
RX(113) OF 531 - 4 STEPS



(step 4)

1. PhMe
2.1. DMF, POCl3
2.2. DMF
3. THF, DMF
4. THF, DMF

RX(113) OF 531 - 4 STEPS

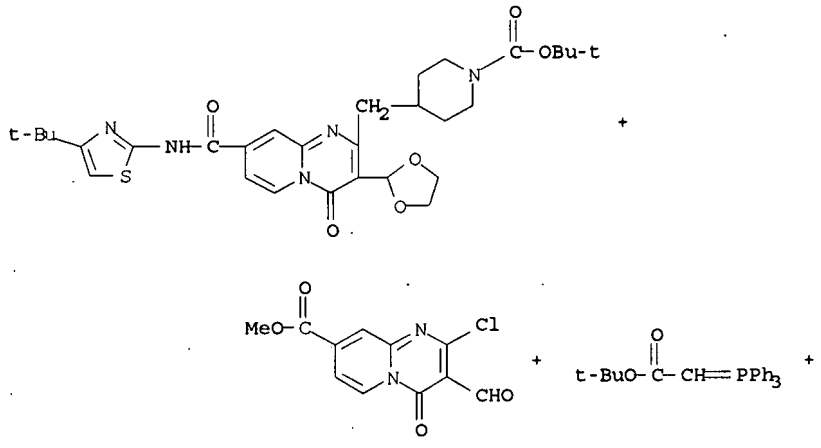


87%

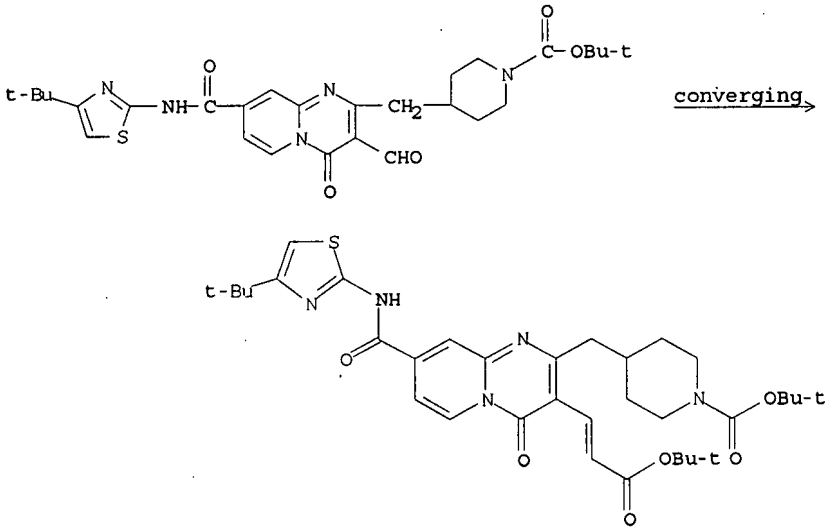
NOTE: 2) Vilsmeier-Haack reaction, 3) Wittig reaction, stereoselective, 4) Wittig reaction, stereoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature

RX(121) OF 531 - 3 STEPS

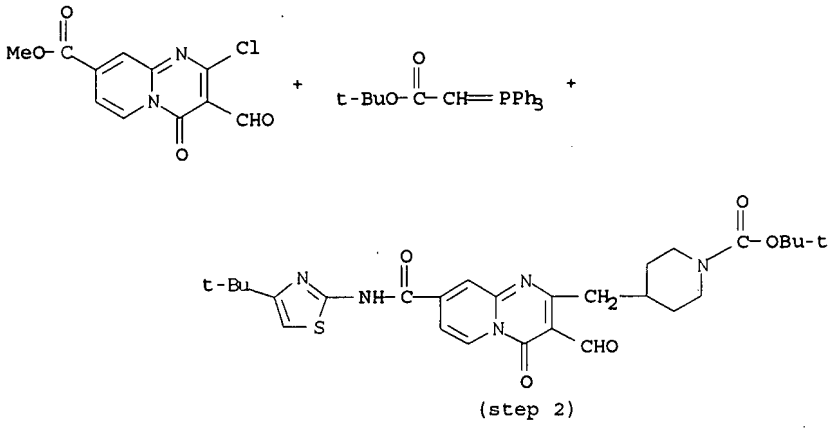


RX(121) OF 531 - 3 STEPS

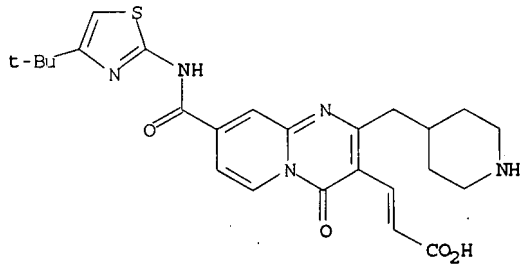


NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 1 hour, 0 deg C

RX(122) OF 531 - 3 STEPS



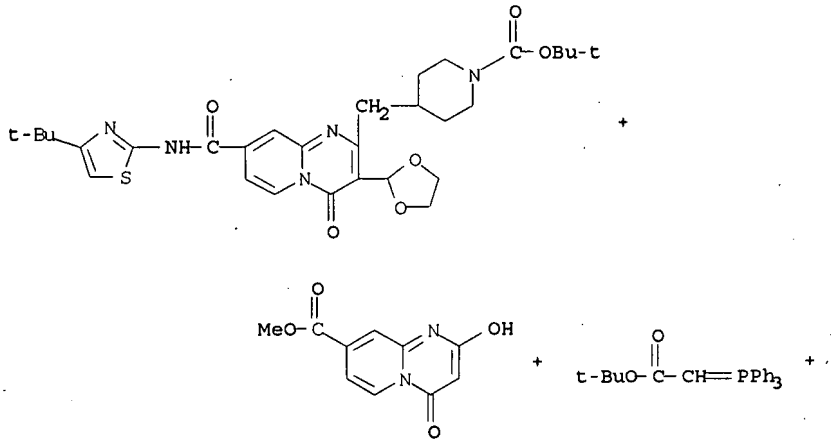
RX(122) OF 531 - 3 STEPS



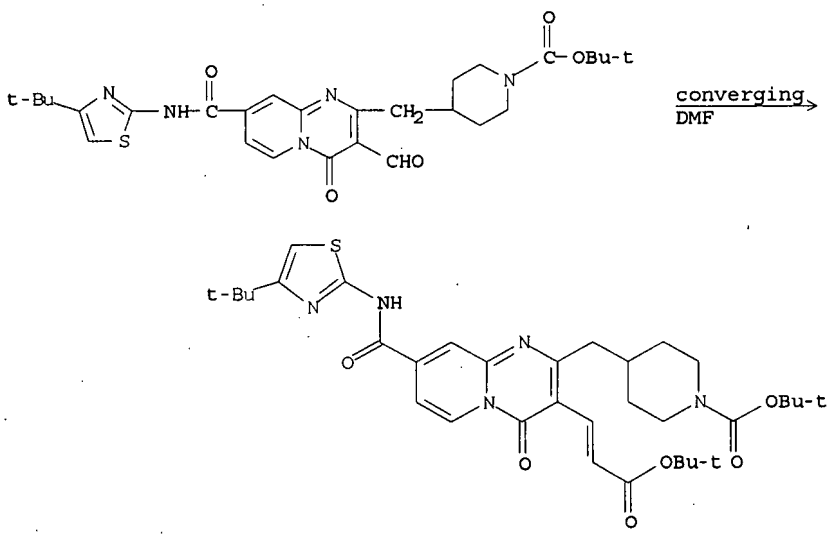
65%

NOTE: 1) Wittig reaction, stereoselective, 2) Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature

RX(127) OF 531 - 4 STEPS



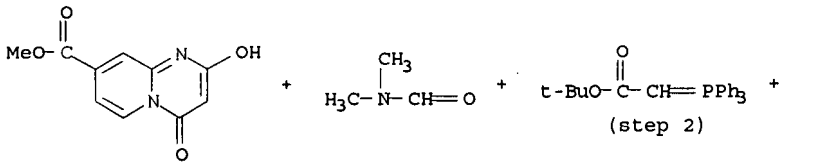
RX(127) OF 531 - 4 STEPS



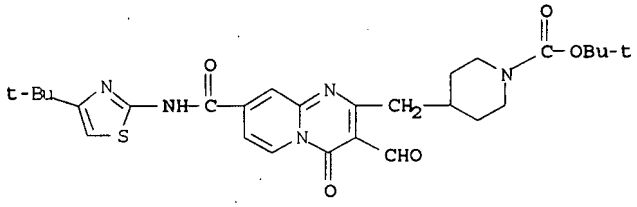
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective
CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 1 hour, 0 deg C

RX(128) OF 531 - 4 STEPS



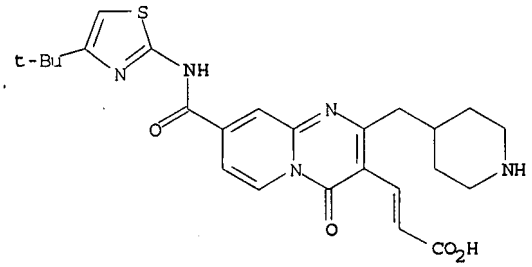
(step 2)



(step 3)

RX(128) OF 531 - 4 STEPS

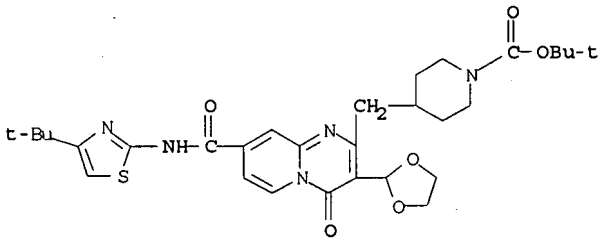
1.1. POCl3
1.2. DMF
2. THF, DMF
3. THF, DMF
4. F3CCO2H



65%

NOTE: 1) Vilsmeier-Haack reaction, 2) Wittig reaction, stereoselective, 3) Wittig reaction, stereoselective
CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 30 minutes, room temperature

RX(178) OF 531 - 3 STEPS



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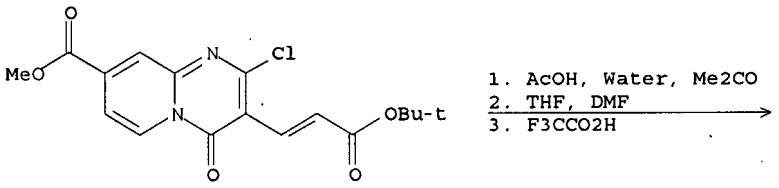
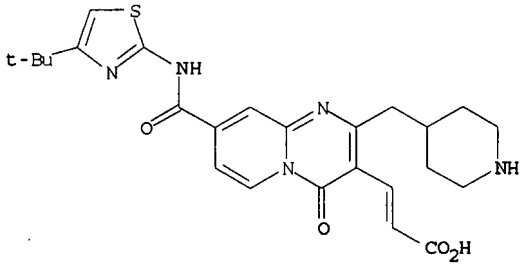


(step 2)

1. AcOH, Water, Me2CO
2. THF, DMF
3. F3CCO2H

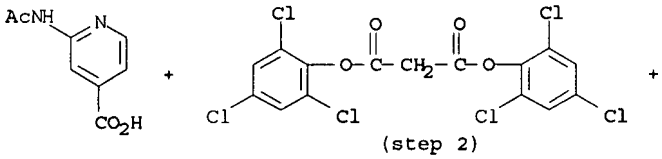
RX(178) OF 531 - 3 STEPS



65%

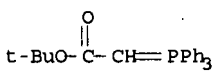
NOTE: 2) Wittig reaction, stereoselective
CON: STEP(1) 1 hour, 0 deg C
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature

RX(195) OF 531 - 5 STEPS



(step 2)

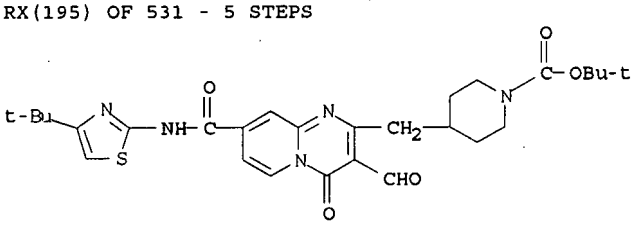
+



(step 4)

+

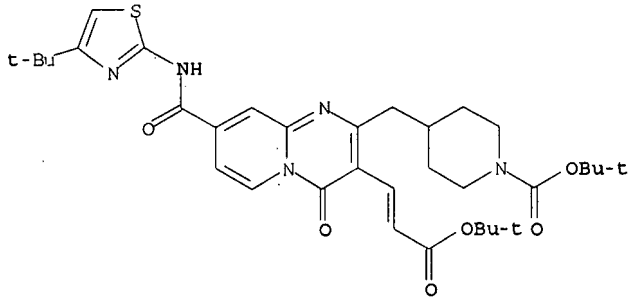
RX(195) OF 531 - 5 STEPS



(step 5)

1. MeOH, SOCl2
2. PhMe
3.1. DMF, POCl3
3.2. DMF
4. THF, DMF
5. THF, DMF

RX(195) OF 531 - 5 STEPS

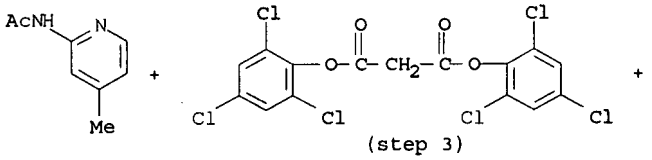


87%

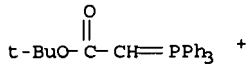
NOTE: 3) Vilsmeier-Haack reaction, 4) Wittig reaction, stereoselective,
5) Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature

RX(203) OF 531 - 6 STEPS

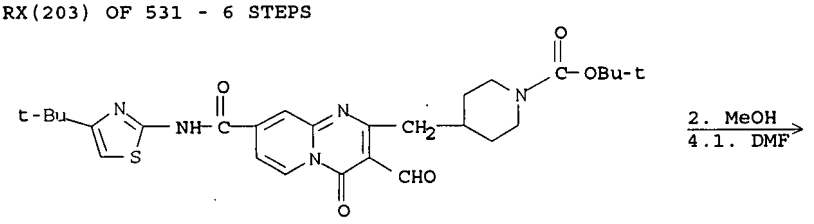


(step 3)



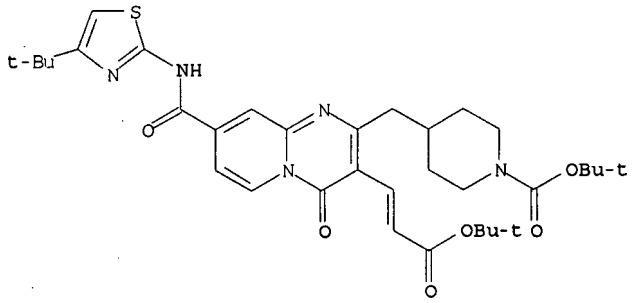
(step 5)

RX(203) OF 531 - 6 STEPS



(step 6)

RX(203) OF 531 - 6 STEPS

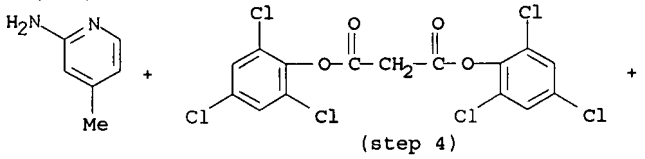


87%

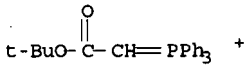
NOTE: 4) Vilsmeier-Haack reaction, 5) Wittig reaction, stereoselective, 6) Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature

RX(211) OF 531 - 7 STEPS

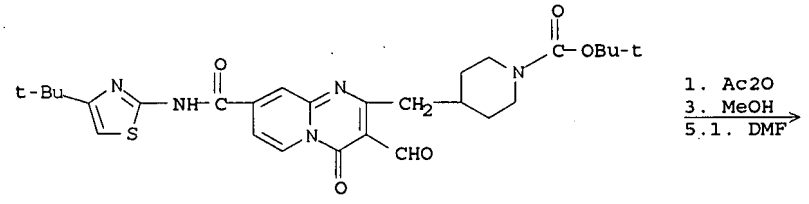


(step 4)



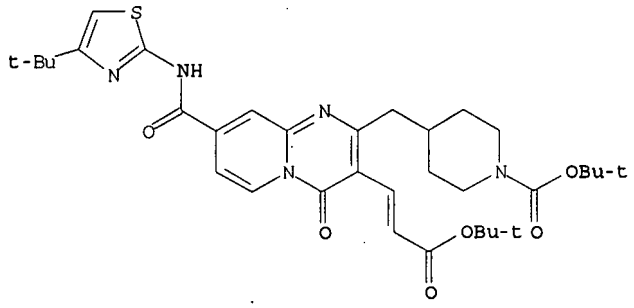
(step 6)

RX(211) OF 531 - 7 STEPS



(step 7)

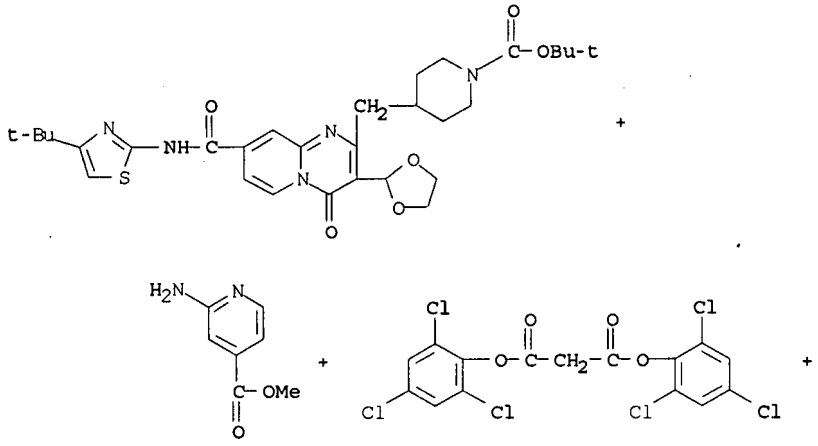
RX(211) OF 531 - 7 STEPS



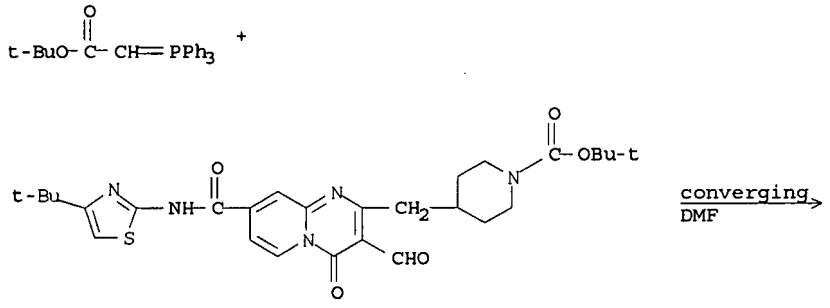
87%

NOTE: 5) Vilsmeier-Haack reaction, 6) Wittig reaction, stereoselective,
7) Wittig reaction, stereoselective
CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature

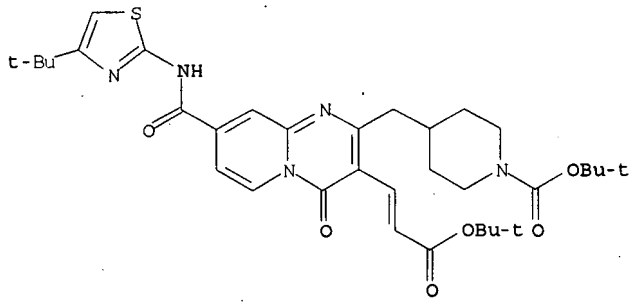
RX(219) OF 531 - 5 STEPS



RX(219) OF 531 - 5 STEPS



RX(219) OF 531 - 5 STEPS

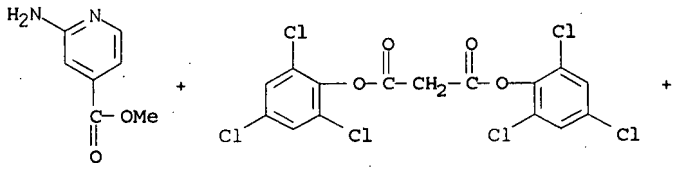


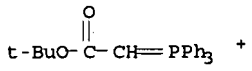
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 1 hour, 0 deg C

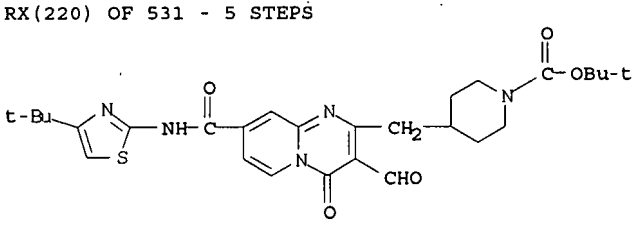
RX(220) OF 531 - 5 STEPS





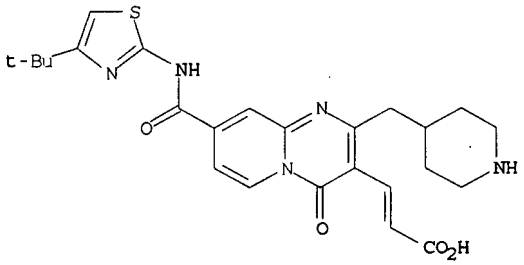
(step 3)

RX(220) OF 531 - 5 STEPS



(step 4)

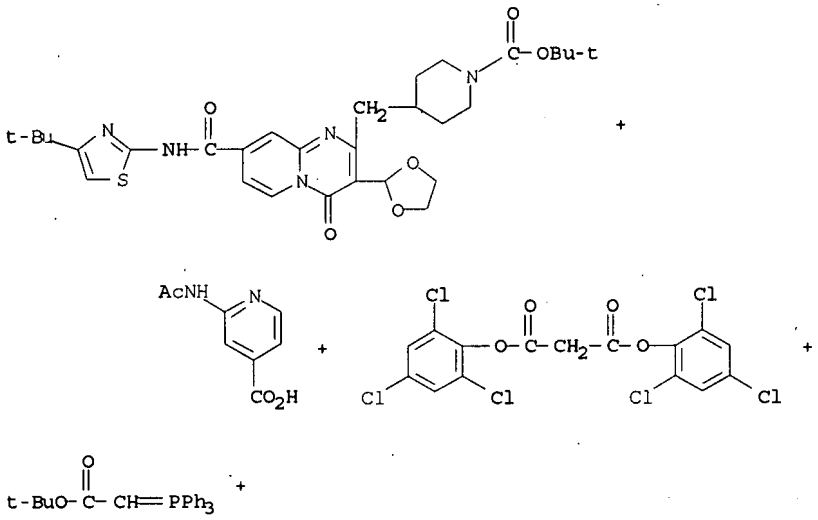
1. PhMe
2.1. DMF, POCl3
2.2. DMF
3. THF, DMF
4. THF, DMF
5. F3CCO2H



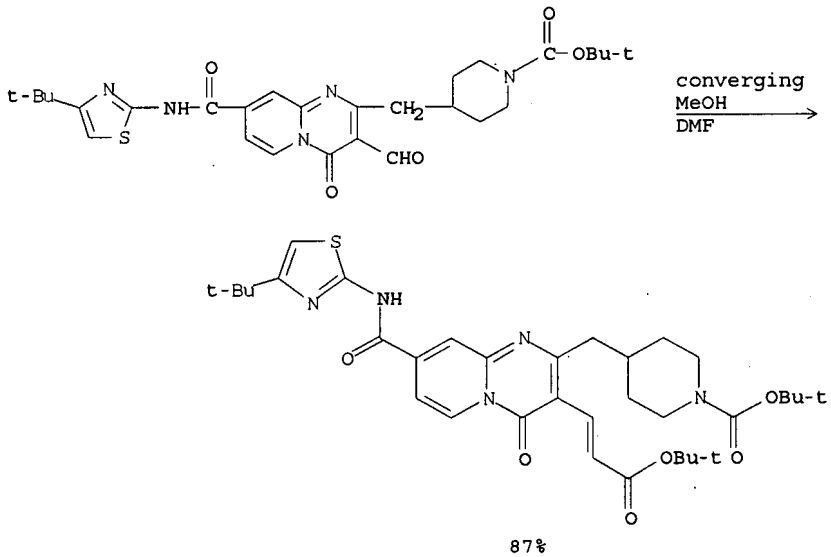
65%

NOTE: 2) Vilsmeier-Haack reaction, 3) Wittig reaction, stereoselective, 4) Wittig reaction, stereoselective
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature

RX(229) OF 531 - 6 STEPS



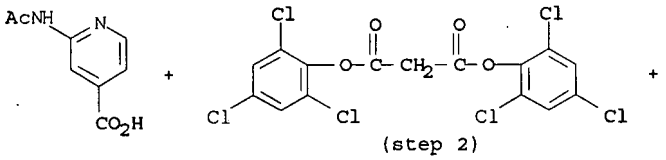
RX(229) OF 531 - 6 STEPS



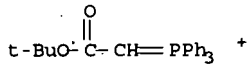
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective,
Wittig reaction, stereoselective
CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 1 hour, 0 deg C

RX(230) OF 531 - 6 STEPS

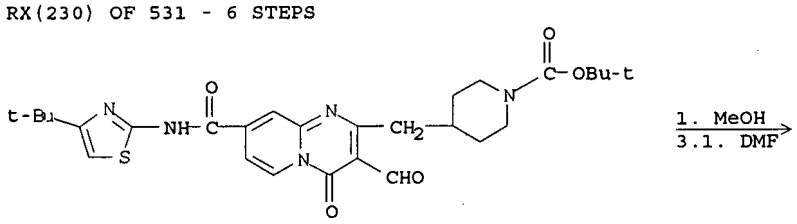


(step 2)

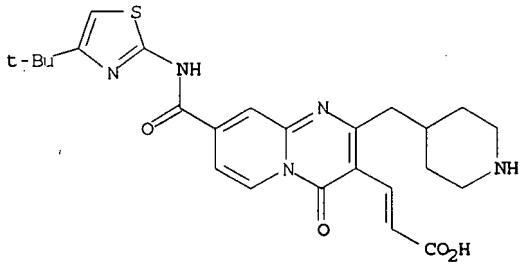


(step 4)

RX(230) OF 531 - 6 STEPS



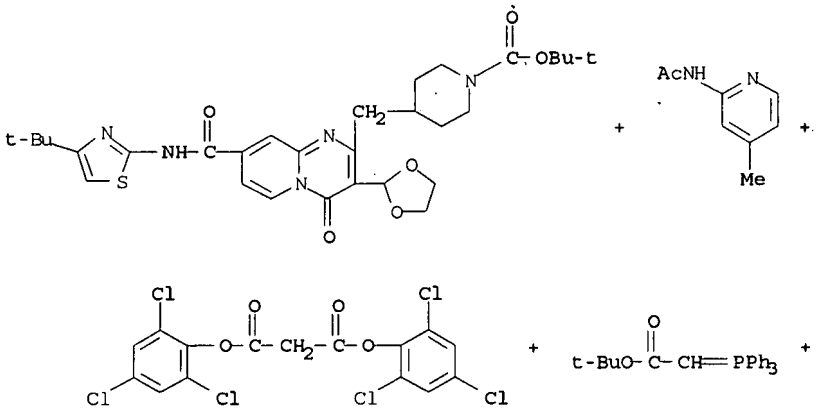
(step 5)



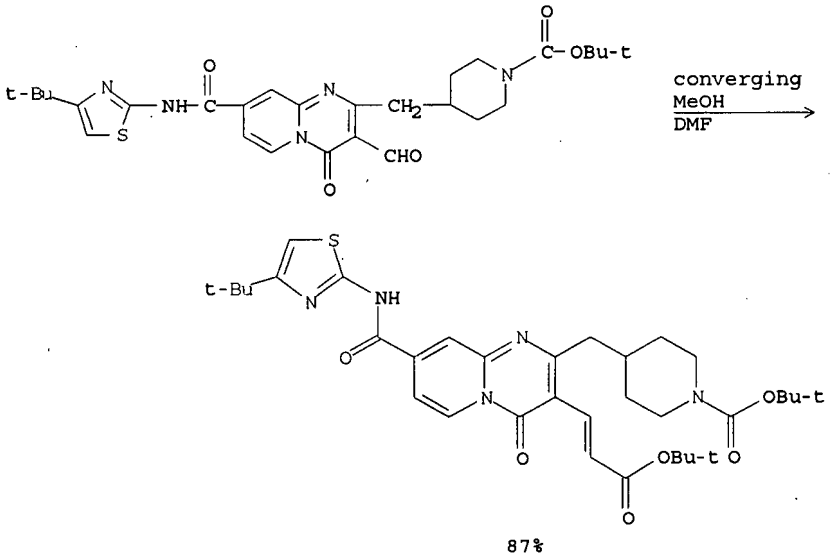
65%

NOTE: 3) Vilsmeier-Haack reaction, 4) Wittig reaction, stereoselective,
5) Wittig reaction, stereoselective
CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature

RX(239) OF 531 - 7 STEPS



RX(239) OF 531 - 7 STEPS

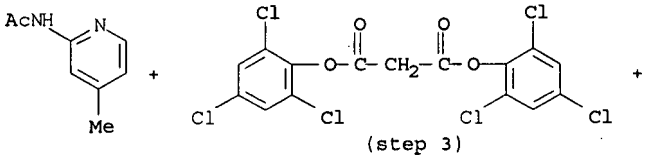


87%

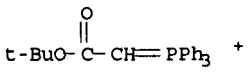
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 1 hour, 0 deg C

RX(240) OF 531 - 7 STEPS

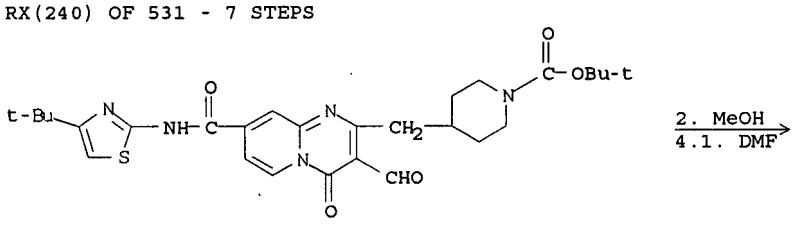


(step 3)

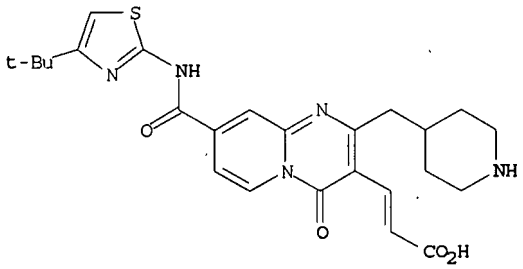


(step 5)

RX(240) OF 531 - 7 STEPS



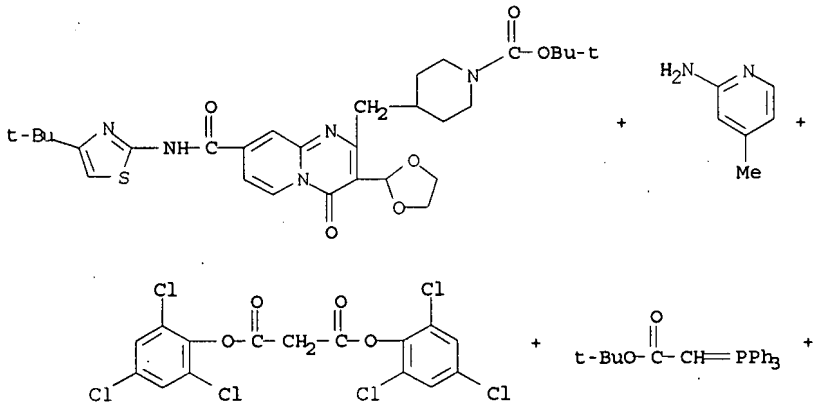
(step 6)



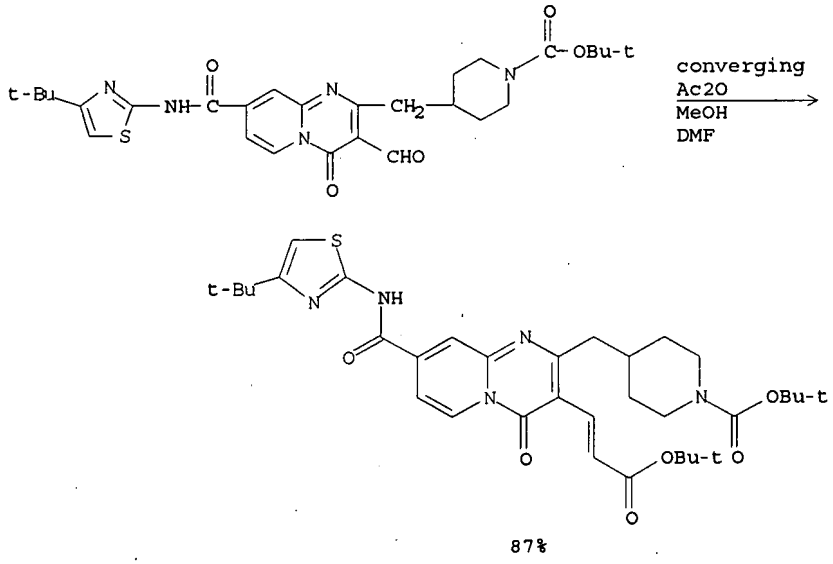
65%

NOTE: 4) Vilsmeier-Haack reaction, 5) Wittig reaction, stereoselective,
6) Wittig reaction, stereoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature

RX(249) OF 531 - 8 STEPS



RX(249) OF 531 - 8 STEPS

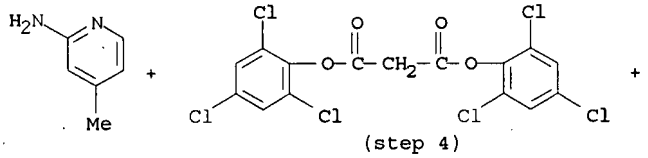


87%

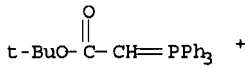
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 1 hour, 0 deg C

RX(250) OF 531 - 8 STEPS

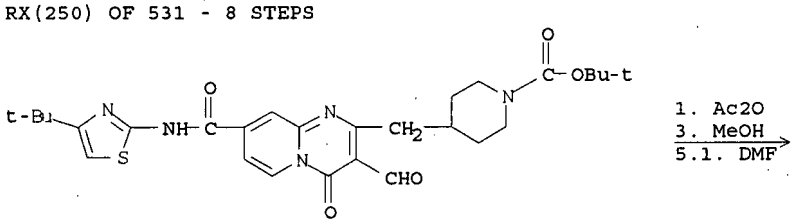


(step 4)

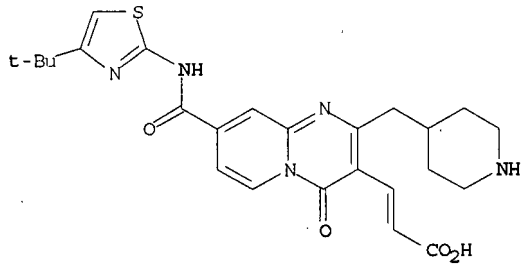


(step 6)

RX(250) OF 531 - 8 STEPS



(step 7)

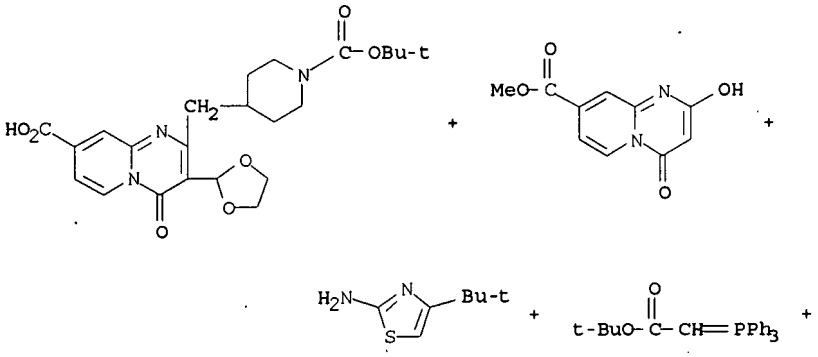


65%

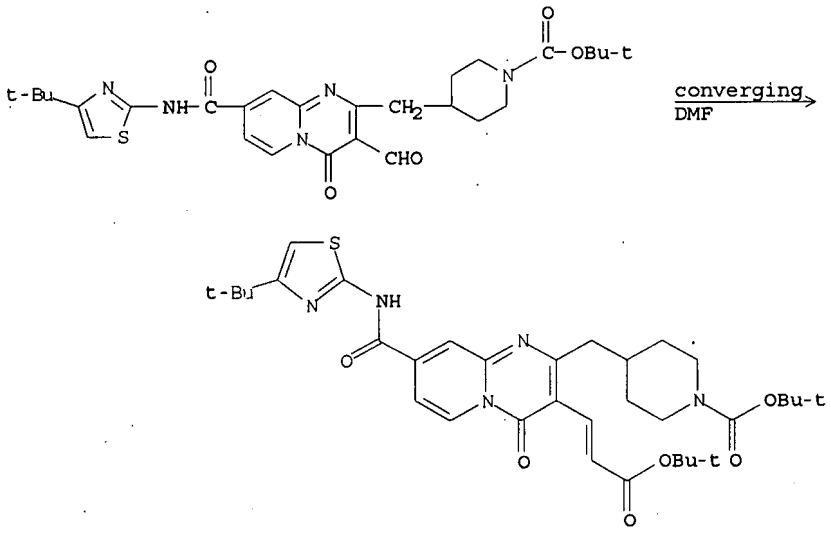
NOTE: 5) Vilsmeier-Haack reaction, 6) Wittig reaction, stereoselective,
7) Wittig reaction, stereoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature

RX(262) OF 531 - 5 STEPS



RX(262) OF 531 - 5 STEPS

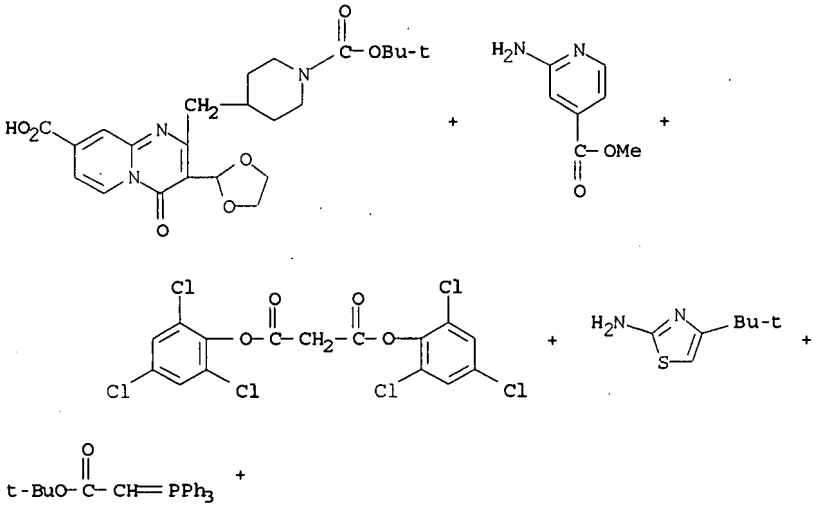


87%

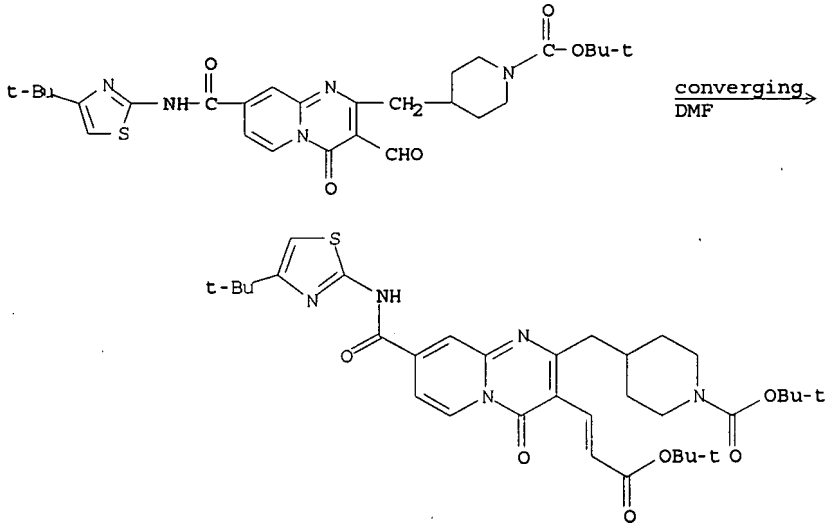
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 12.5 hours, room temperature
STEP(5) 1 hour, 0 deg C

RX(270) OF 531 - 6 STEPS



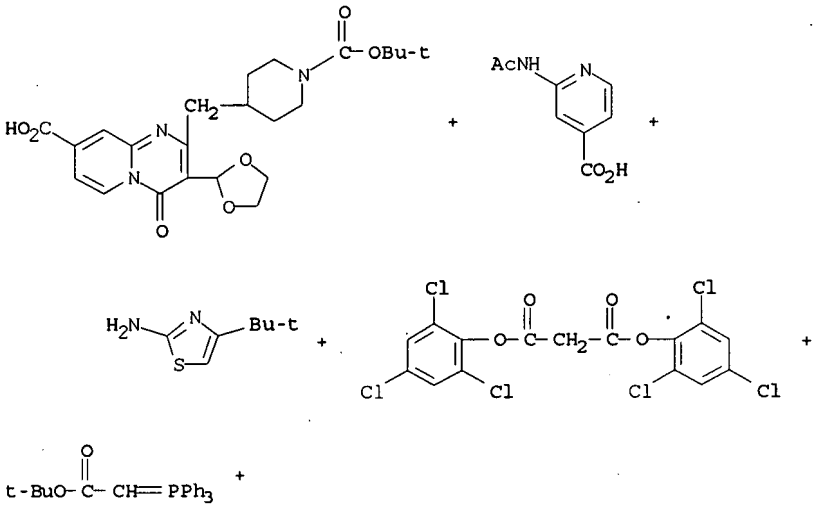
RX(270) OF 531 - 6 STEPS



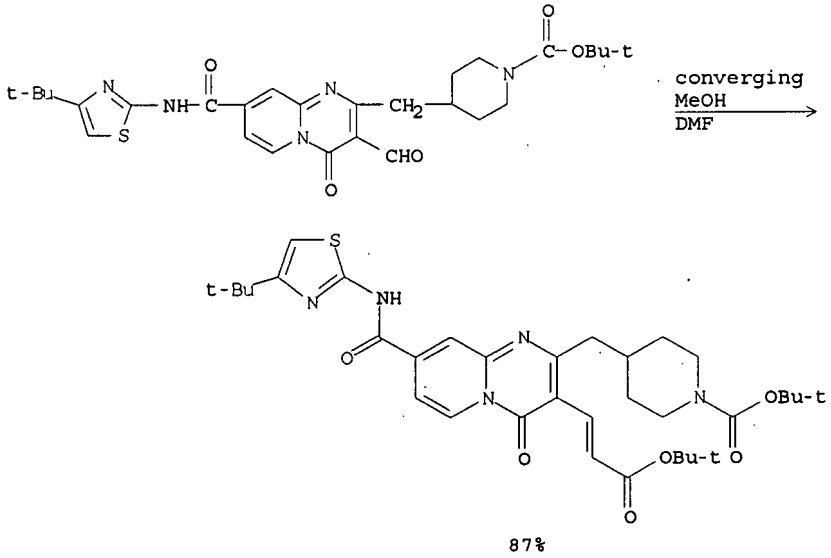
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective,
Wittig reaction, stereoselective
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 12.5 hours, room temperature
STEP(6) 1 hour, 0 deg C

RX(278) OF 531 - 7 STEPS



RX(278) OF 531 - 7 STEPS

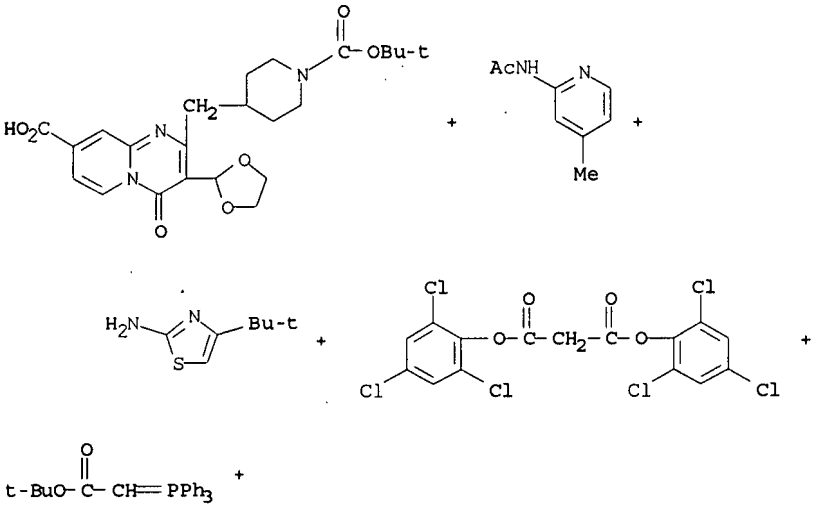


87%

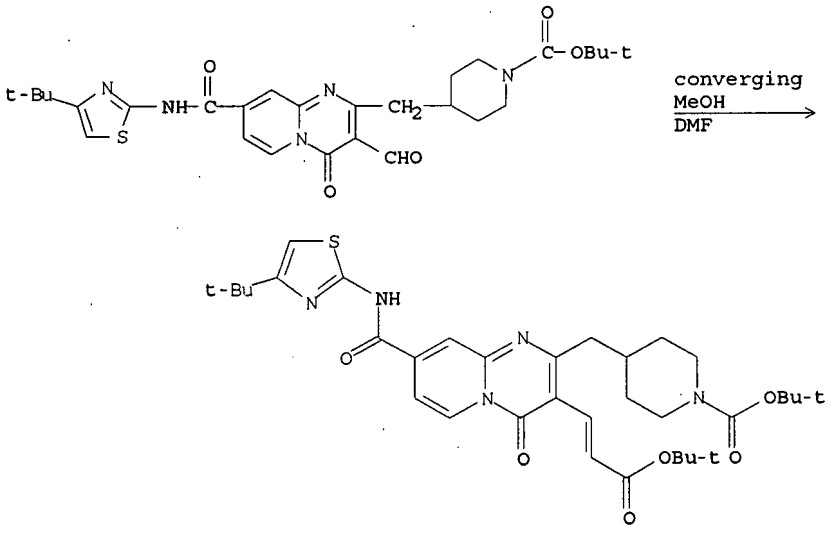
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 12.5 hours, room temperature
STEP(7) 1 hour, 0 deg C

RX(286) OF 531 - 8 STEPS



RX(286) OF 531 - 8 STEPS

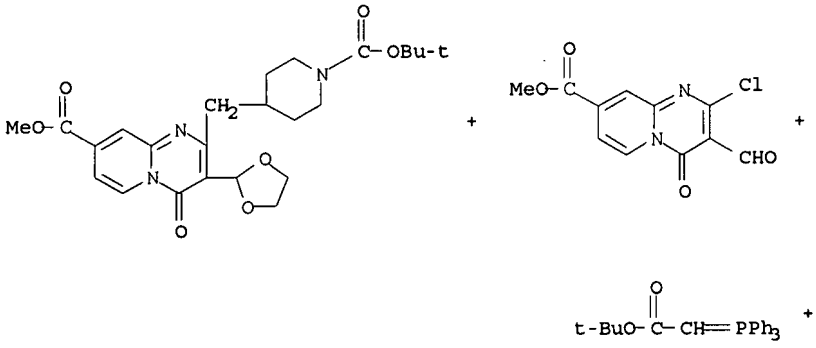


87%

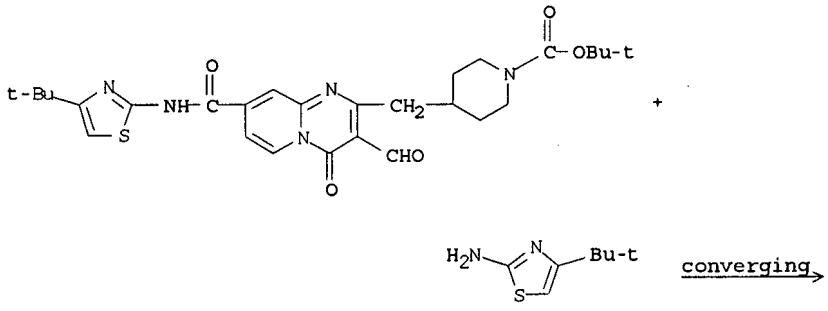
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 12.5 hours, room temperature
STEP(8) 1 hour, 0 deg C

RX(290) OF 531 - 5 STEPS

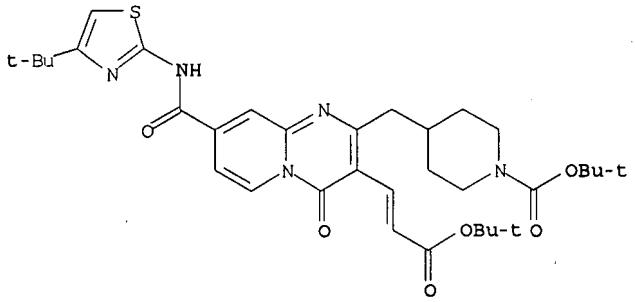


RX(290) OF 531 - 5 STEPS



converging

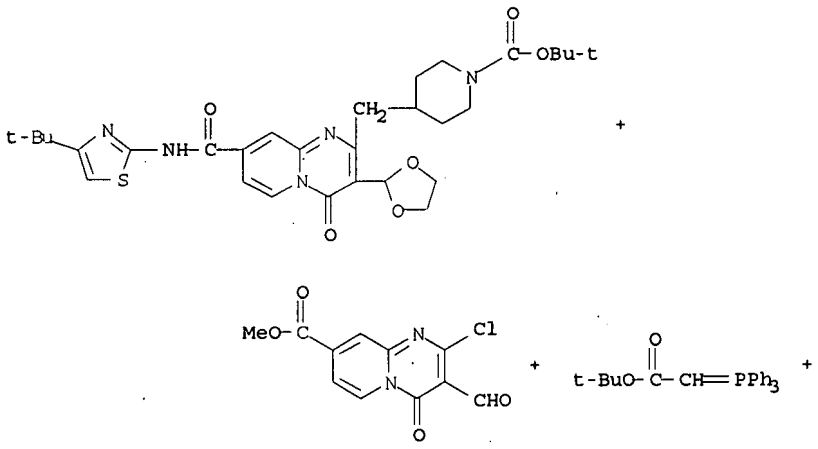
RX(290) OF 531 - 5 STEPS



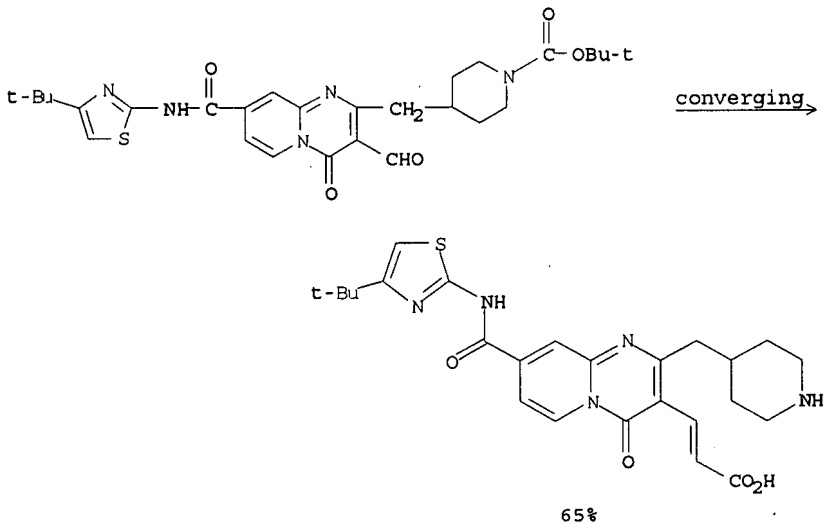
87%

NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3.1) 30 minutes, room temperature
STEP(3.2) room temperature, pH 4
STEP(4) 12.5 hours, room temperature
STEP(5) 1 hour, 0 deg C

RX(291) OF 531 - 4 STEPS



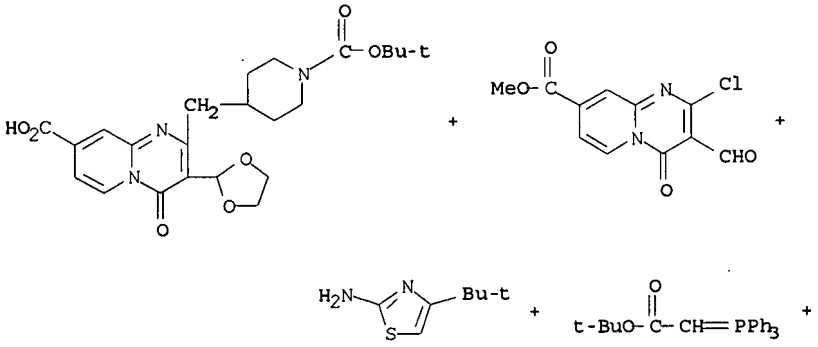
RX(291) OF 531 - 4 STEPS



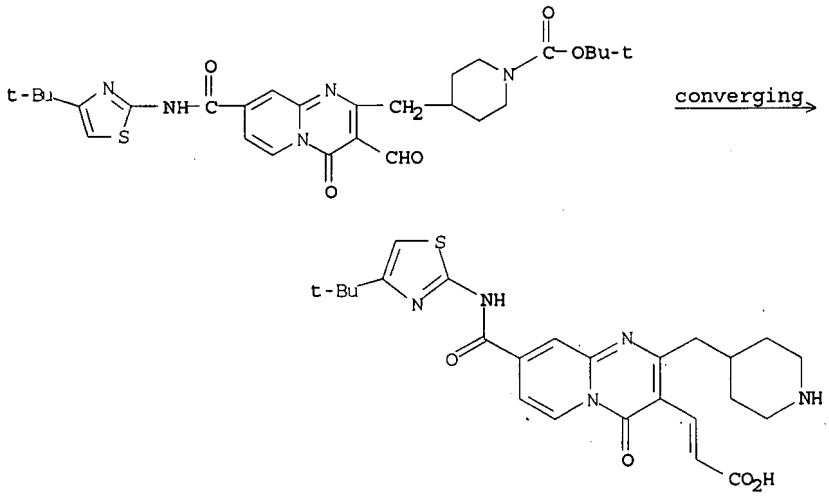
65%

NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature
STEP(4) 1 hour, 0 deg C

RX(292) OF 531 - 5 STEPS



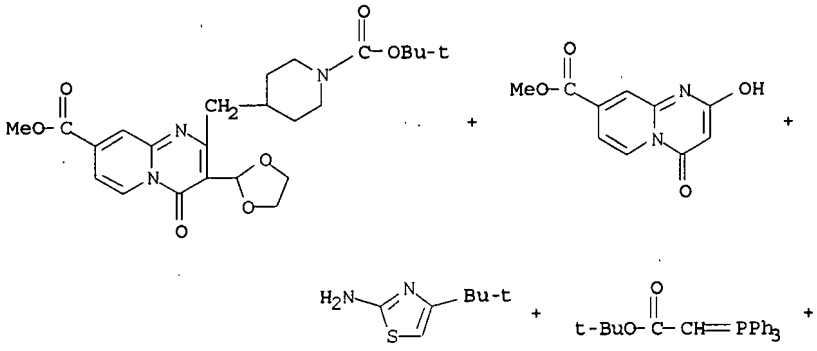
RX(292) OF 531 - 5 STEPS



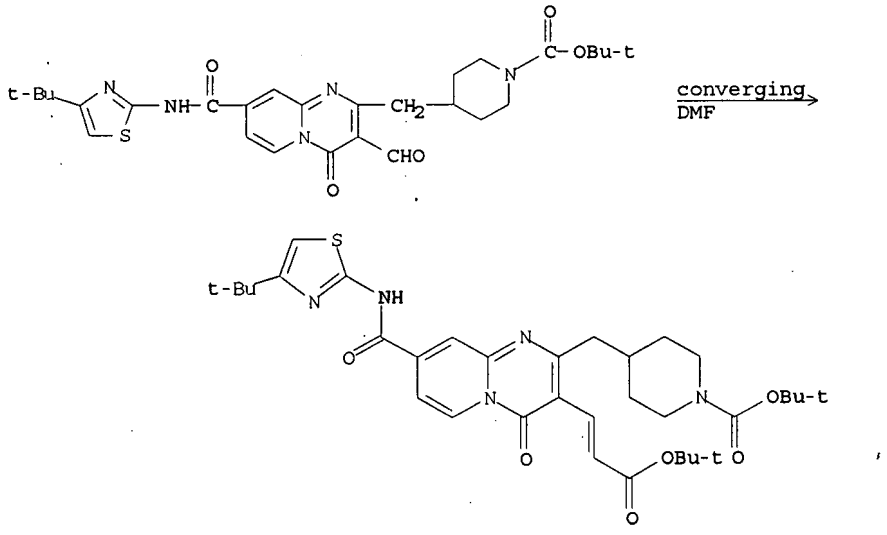
65%

NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective
CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature
STEP(4) 12.5 hours, room temperature
STEP(5) 1 hour, 0 deg C

RX(295) OF 531 - 6 STEPS



RX(295) OF 531 - 6 STEPS

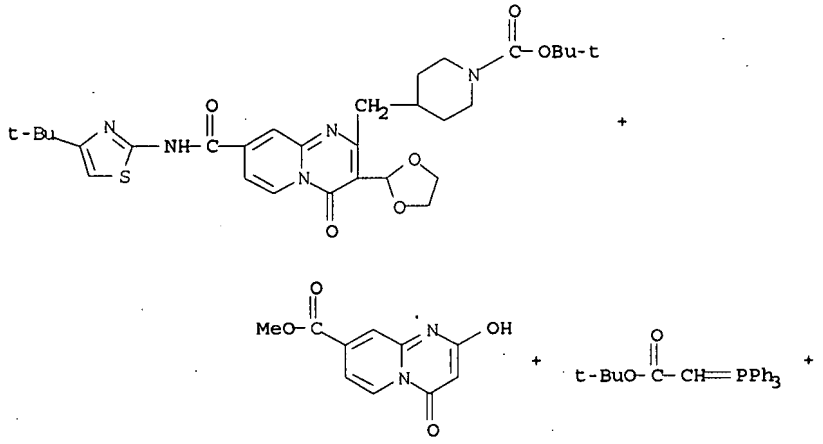


87%

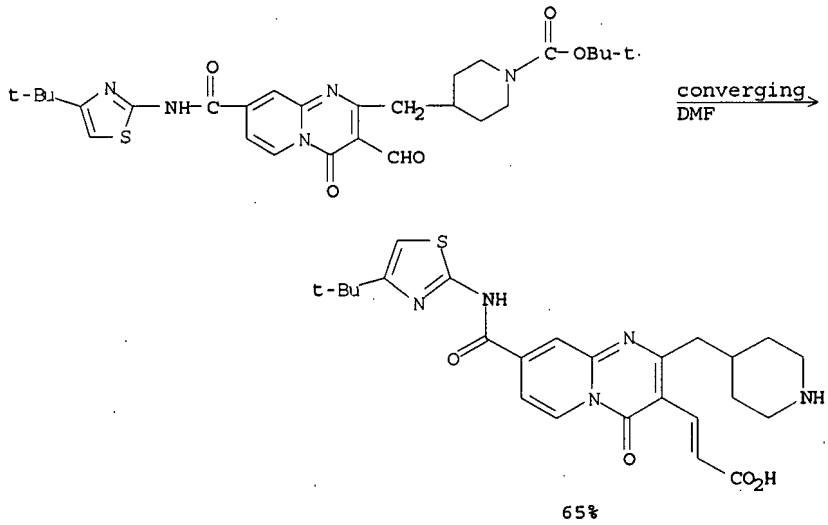
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4.1) 30 minutes, room temperature
STEP(4.2) room temperature, pH 4
STEP(5) 12.5 hours, room temperature
STEP(6) 1 hour, 0 deg C

RX(296) OF 531 - 5 STEPS



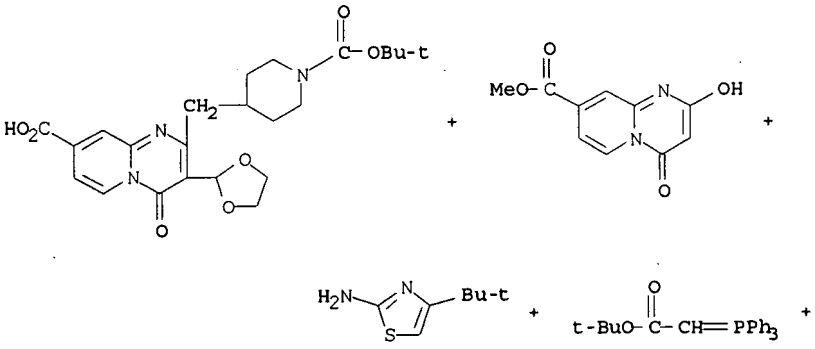
RX(296) OF 531 - 5 STEPS



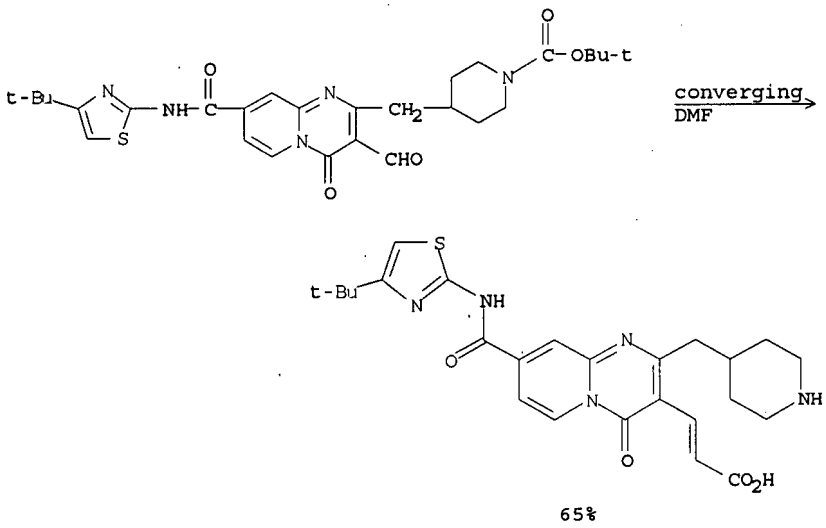
65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective
CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 30 minutes, room temperature
STEP(5) 1 hour, 0 deg C

RX(297) OF 531 - 6 STEPS



RX(297) OF 531 - 6 STEPS

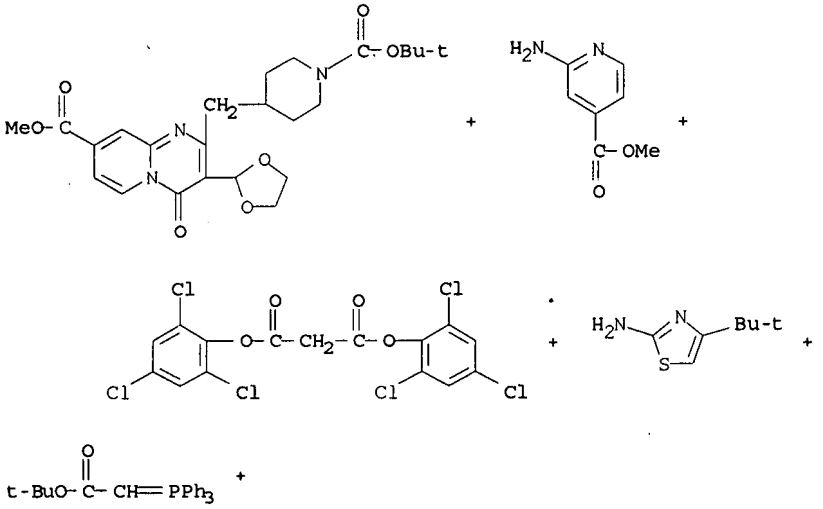


65%

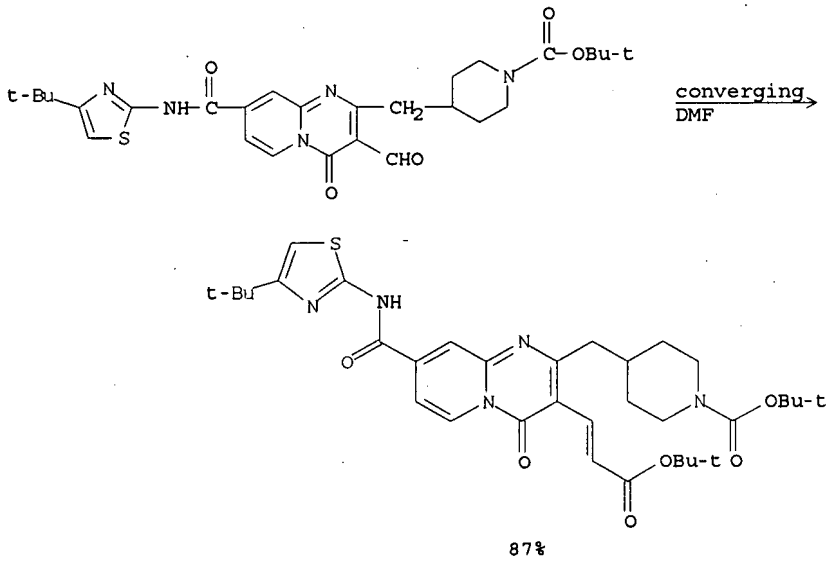
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 30 minutes, room temperature
STEP(5) 12.5 hours, room temperature
STEP(6) 1 hour, 0 deg C

RX(300) OF 531 - 7 STEPS



RX(300) OF 531 - 7 STEPS

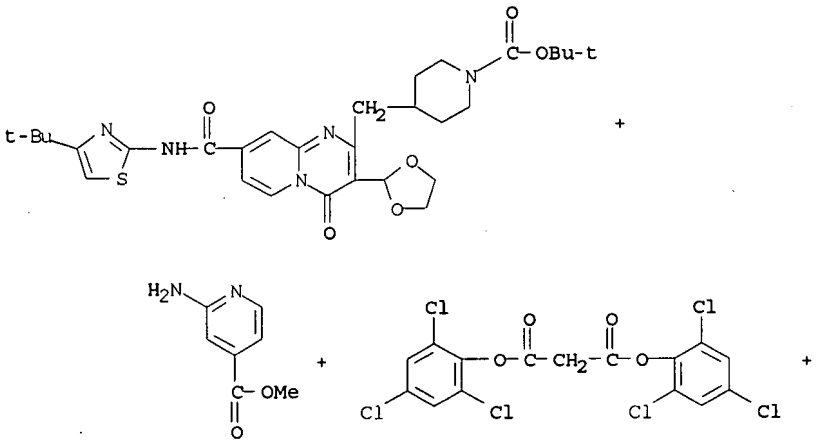


87%

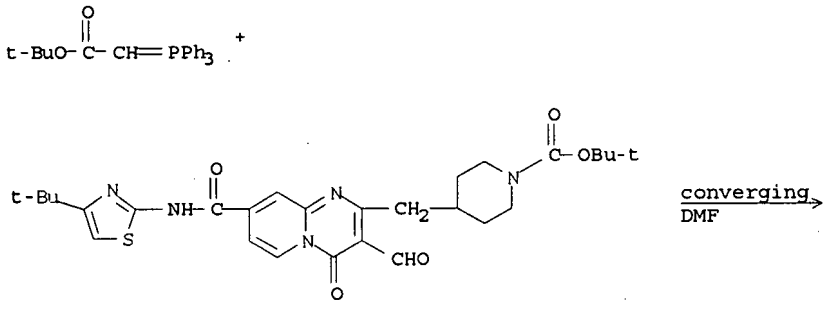
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5.1) 30 minutes, room temperature
STEP(5.2) room temperature, pH 4
STEP(6) 12.5 hours, room temperature
STEP(7) 1 hour, 0 deg C

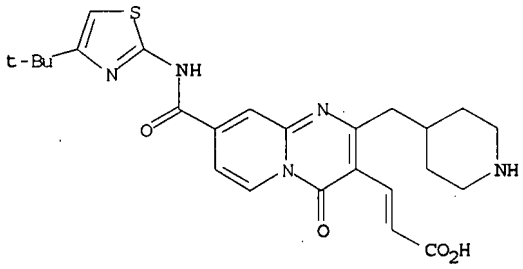
RX(301) OF 531 - 6 STEPS



RX(301) OF 531 - 6 STEPS



RX(301) OF 531 - 6 STEPS

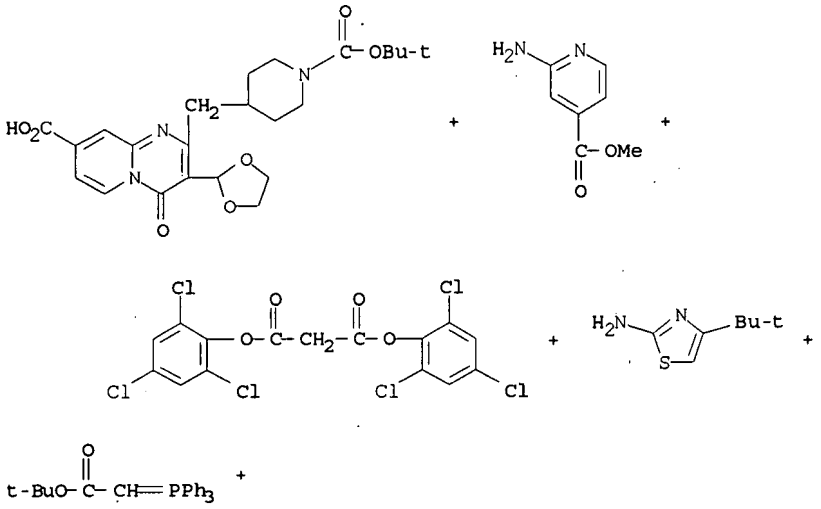


65%

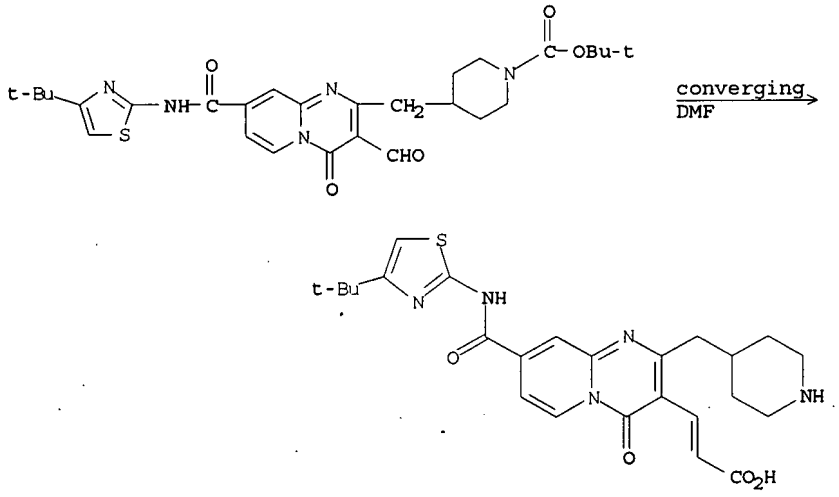
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6) 1 hour, 0 deg C

RX(302) OF 531 - 7 STEPS



RX(302) OF 531 - 7 STEPS

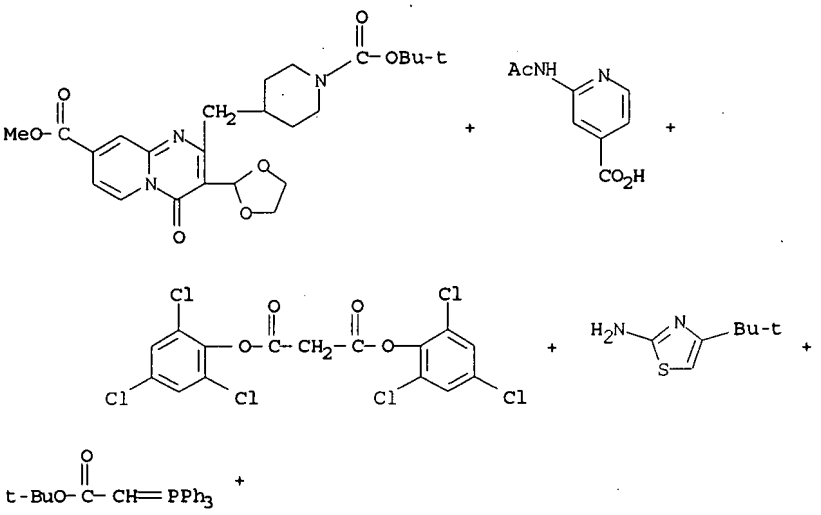


65%

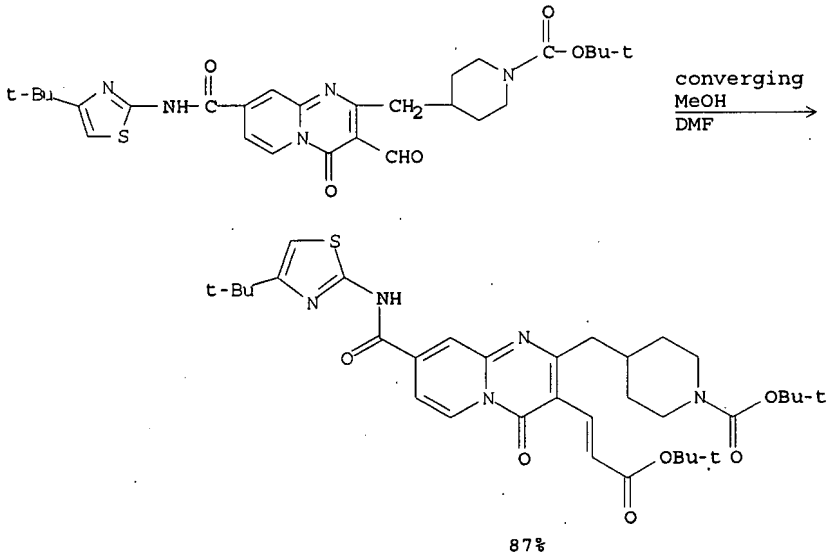
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6) 12.5 hours, room temperature
STEP(7) 1 hour, 0 deg C

RX(305) OF 531 - 8 STEPS



RX(305) OF 531 - 8 STEPS

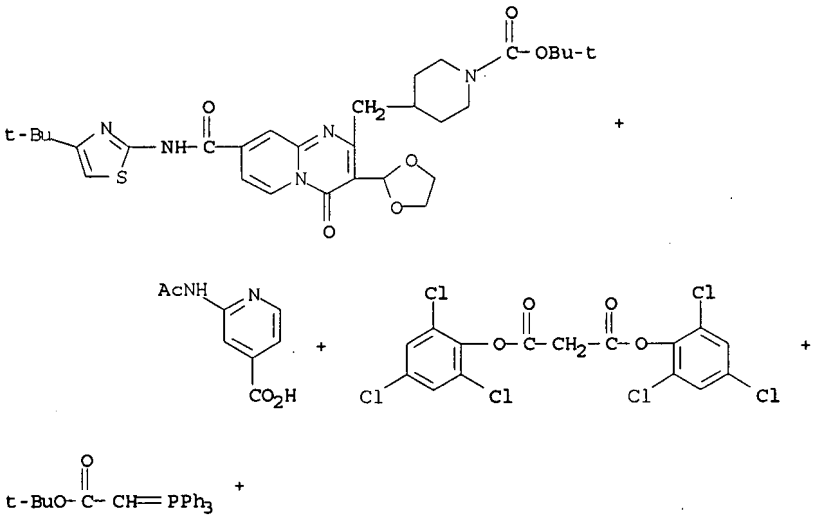


87%

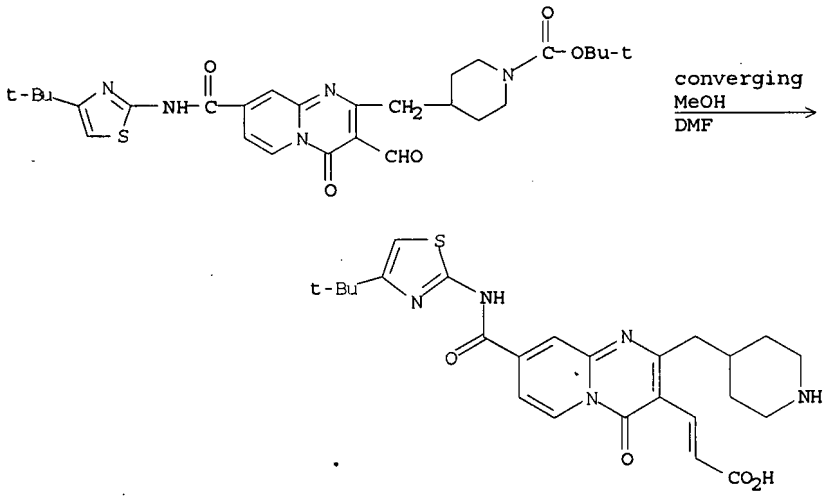
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6.1) 30 minutes, room temperature
STEP(6.2) room temperature, pH 4
STEP(7) 12.5 hours, room temperature
STEP(8) 1 hour, 0 deg C

RX(306) OF 531 - 7 STEPS



RX(306) OF 531 - 7 STEPS

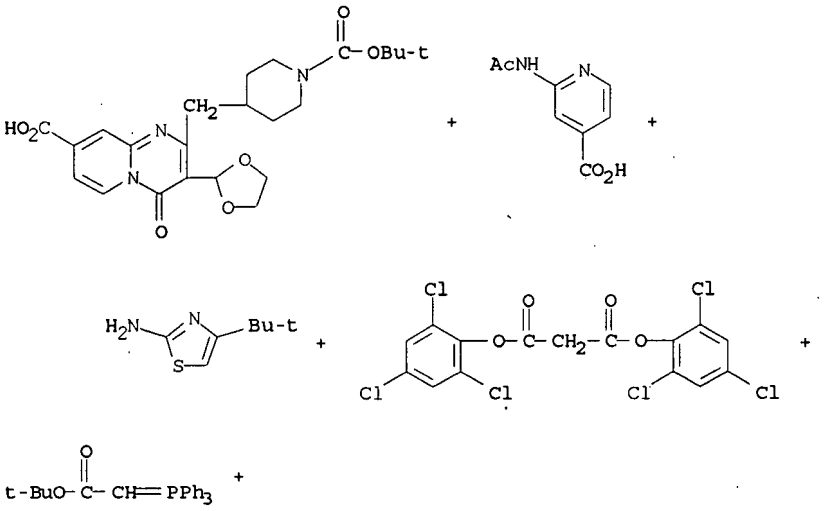


65%

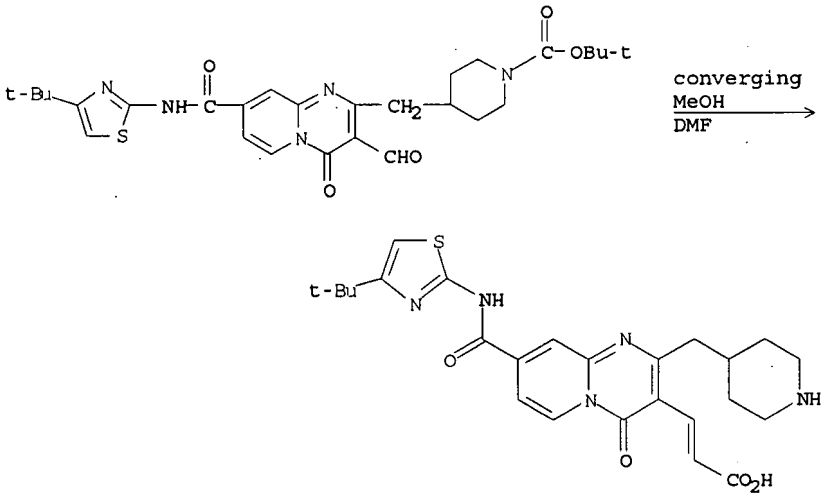
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7) 1 hour, 0 deg C

RX(307) OF 531 - 8 STEPS



RX(307) OF 531 - 8 STEPS

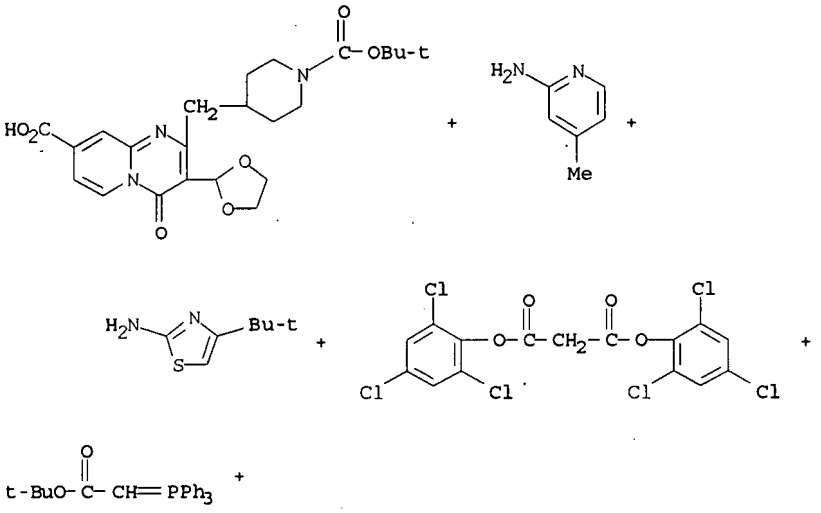


65%

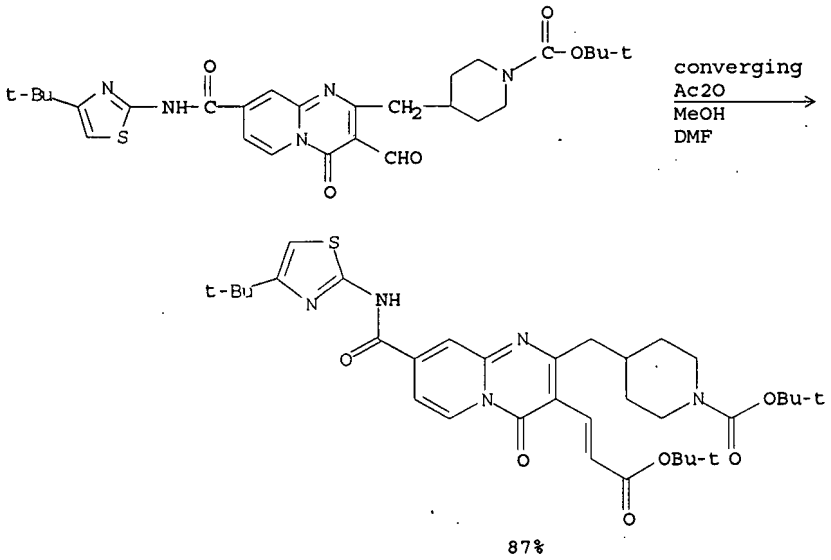
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7) 12.5 hours, room temperature
STEP(8) 1 hour, 0 deg C

RX(384) OF 531 - 9 STEPS



RX(384) OF 531 - 9 STEPS

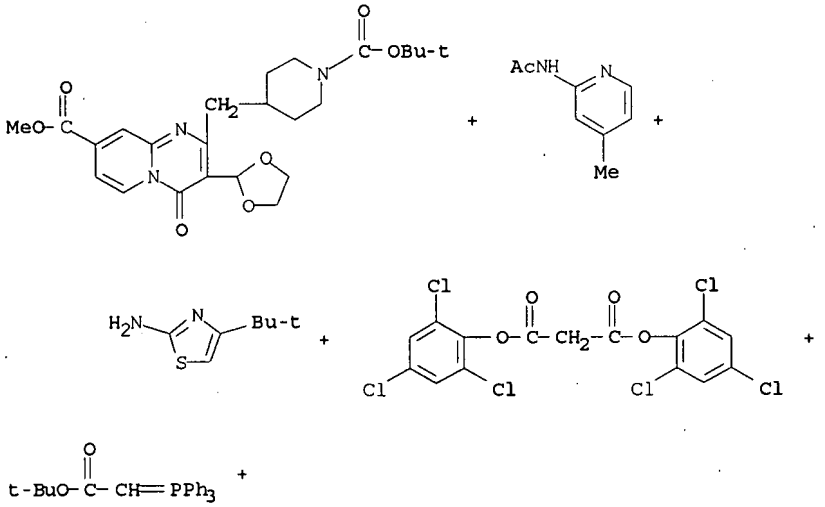


87%

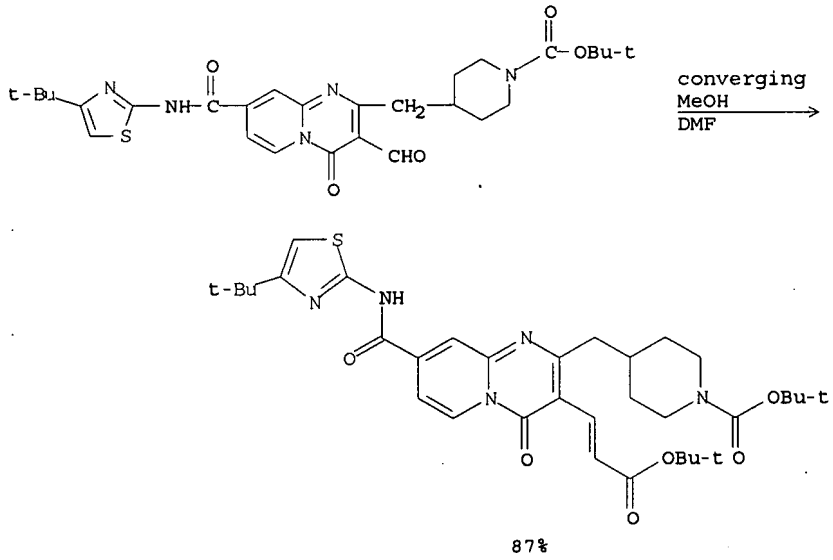
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(388) OF 531 - 9 STEPS



RX(388) OF 531 - 9 STEPS

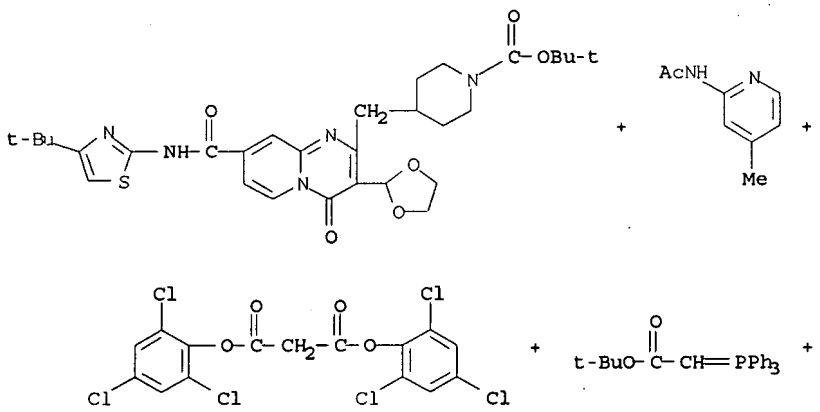


87%

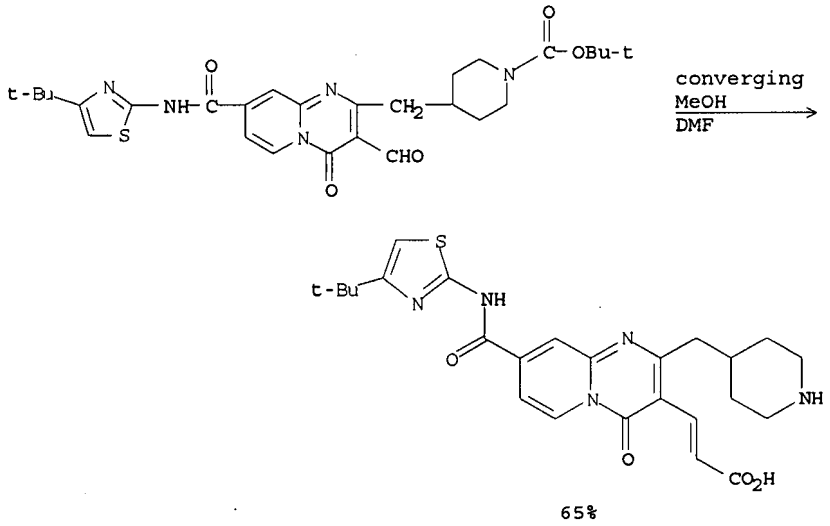
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(389) OF 531 - 8 STEPS



RX(389) OF 531 - 8 STEPS

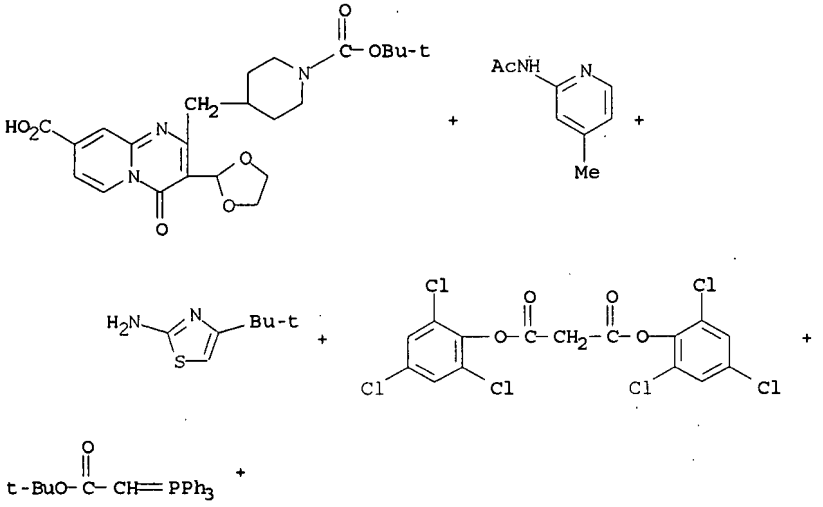


65%

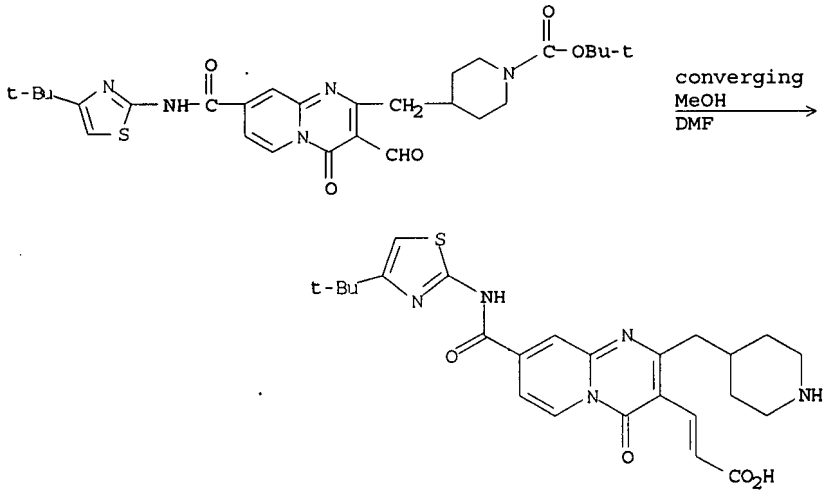
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8) 1 hour, 0 deg C

RX(390) OF 531 - 9 STEPS



RX(390) OF 531 - 9 STEPS

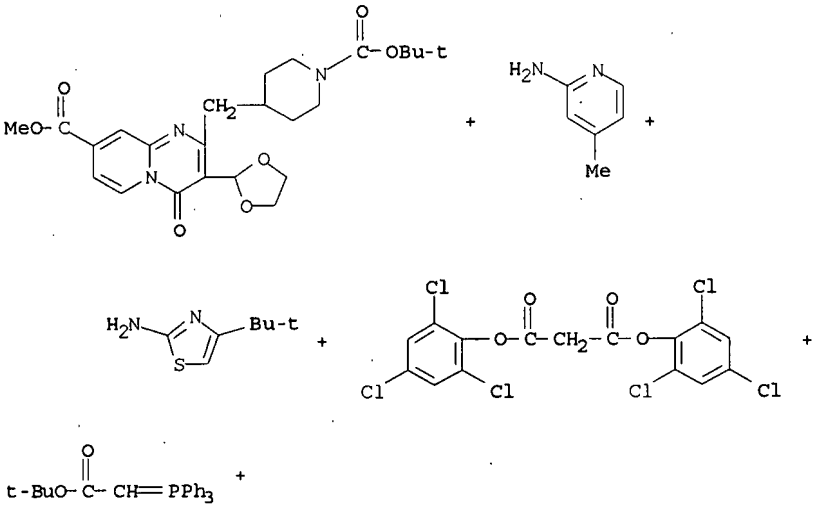


65%

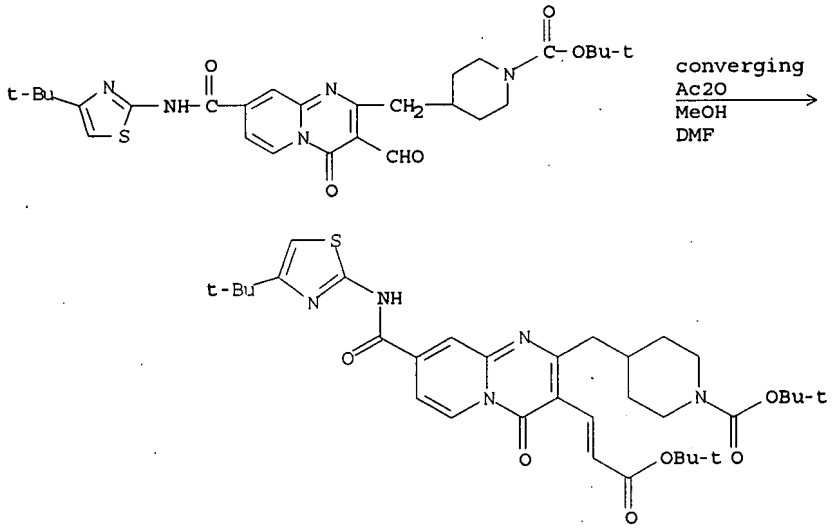
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(397) OF 531 - 10 STEPS



RX(397) OF 531 - 10 STEPS

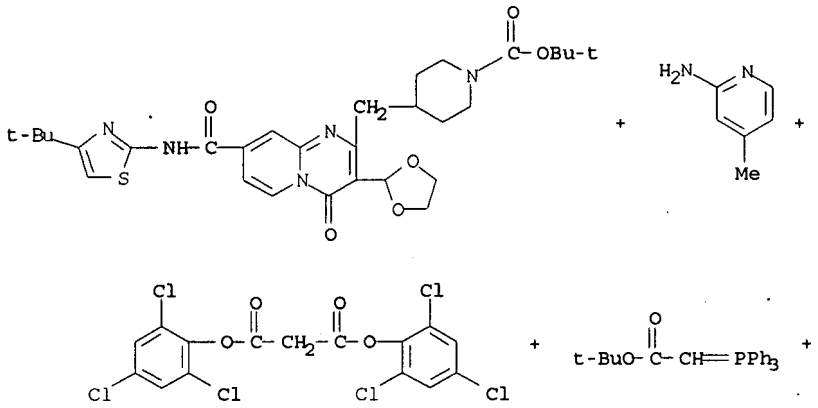


87%

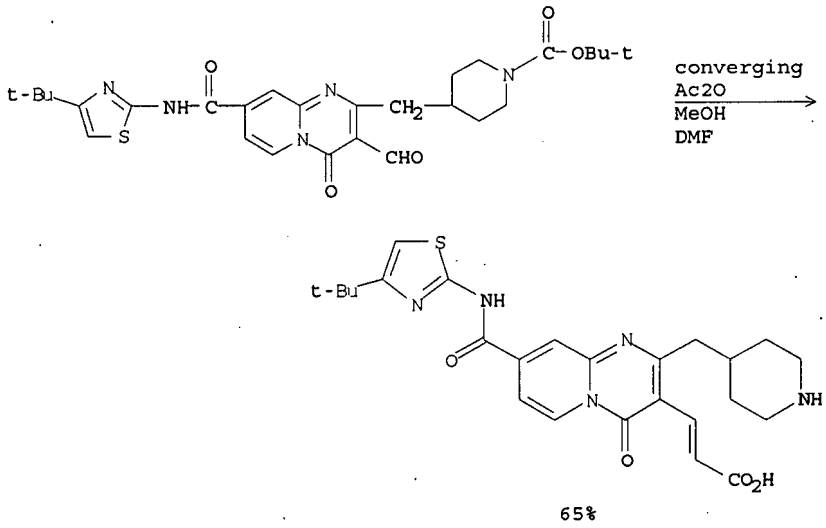
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(398) OF 531 - 9 STEPS



RX(398) OF 531 - 9 STEPS

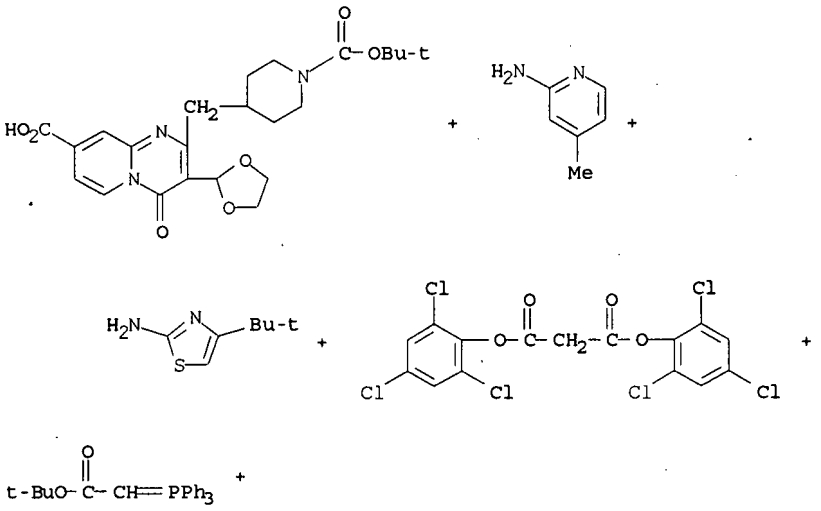


65%

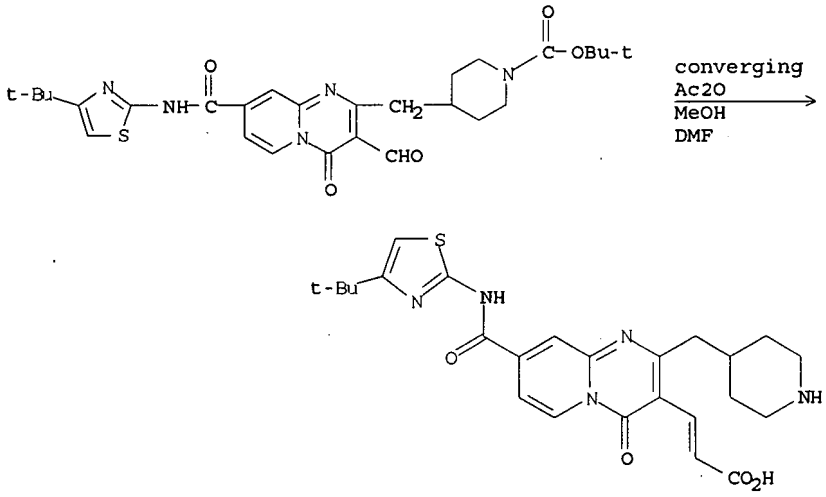
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective,
Wittig reaction, stereoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9) 1 hour, 0 deg C

RX(399) OF 531 - 10 STEPS



RX(399) OF 531 - 10 STEPS

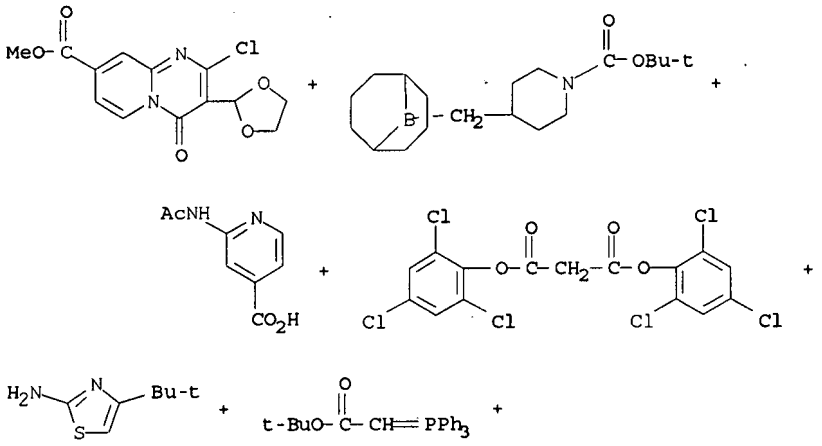


65%

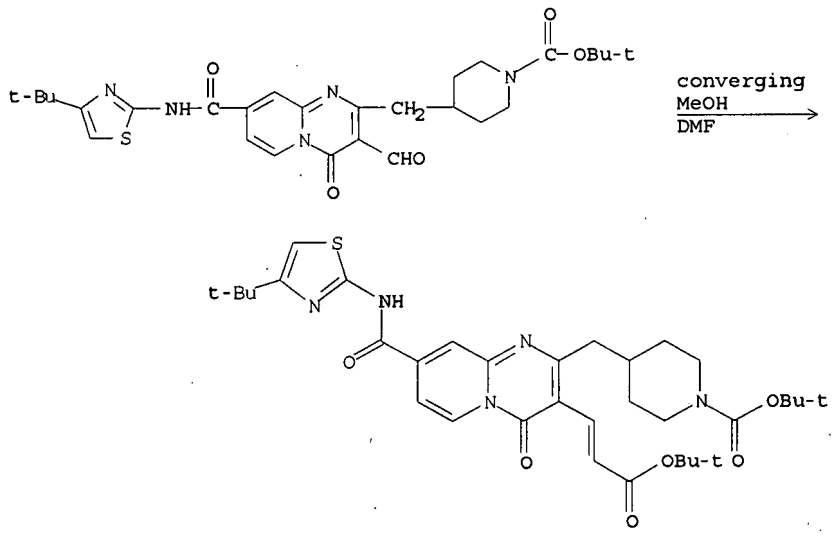
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(407) OF 531 - 9 STEPS



RX(407) OF 531 - 9 STEPS

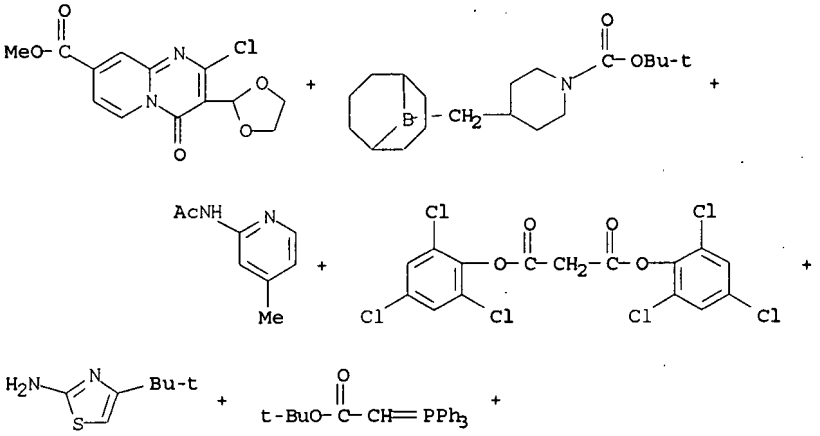


87%

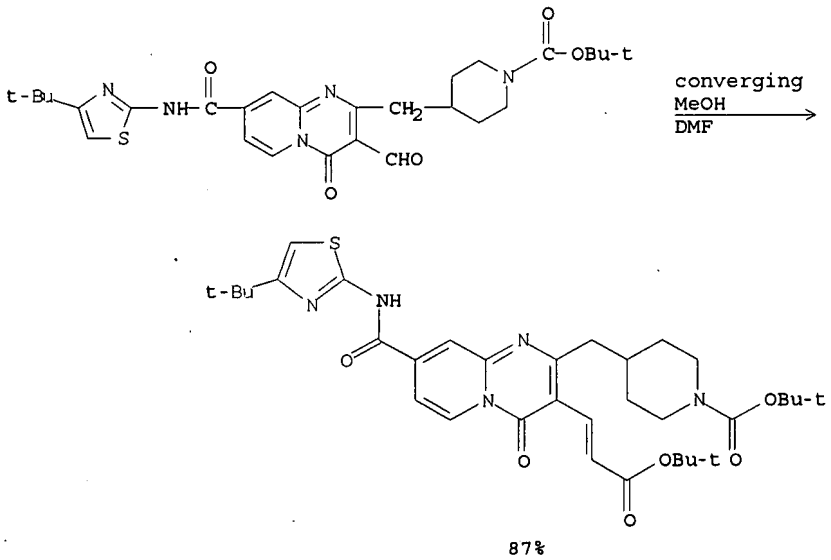
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(411) OF 531 - 10 STEPS



RX(411) OF 531 - 10 STEPS

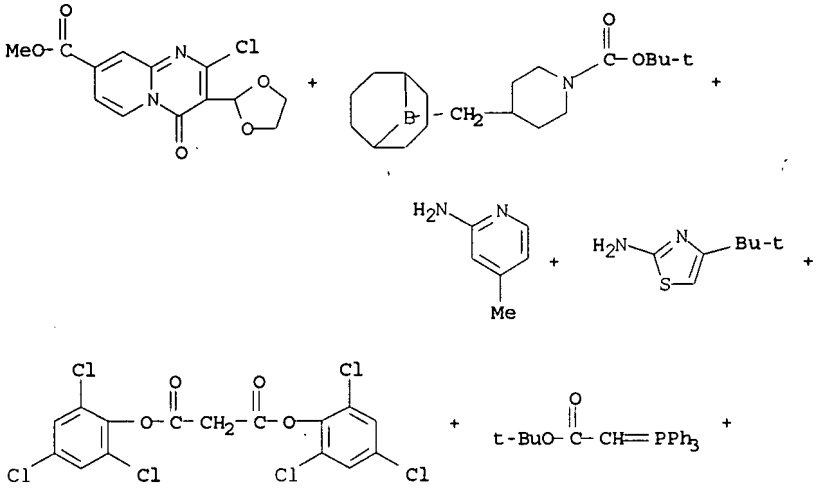


87%

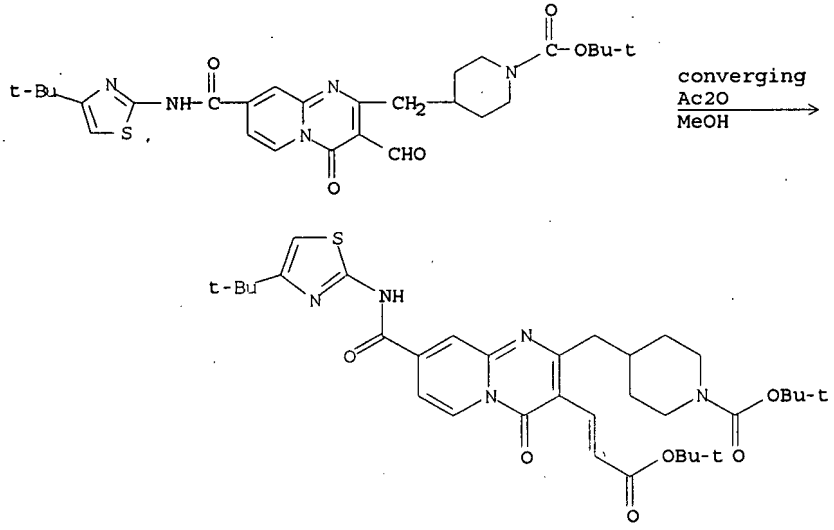
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(415) OF 531 - 11 STEPS



RX(415) OF 531 - 11 STEPS

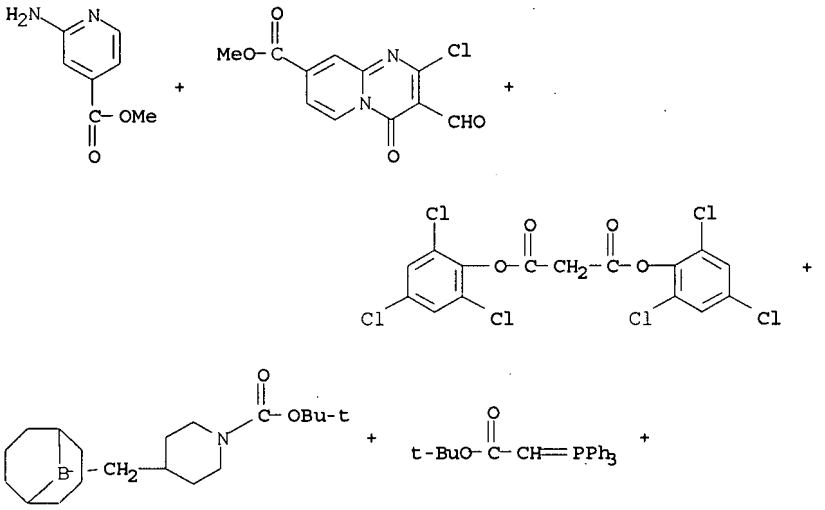


87%

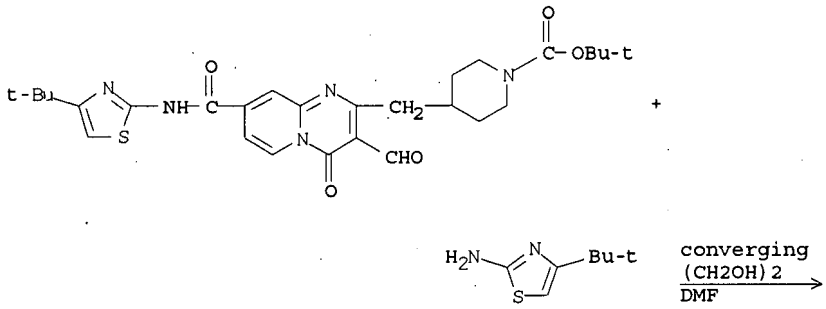
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

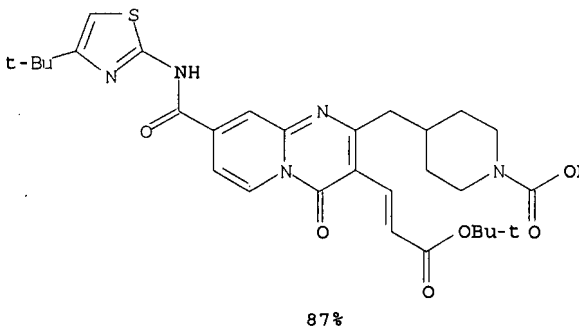
RX(420) OF 531 - 9 STEPS



RX(420) OF 531 - 9 STEPS



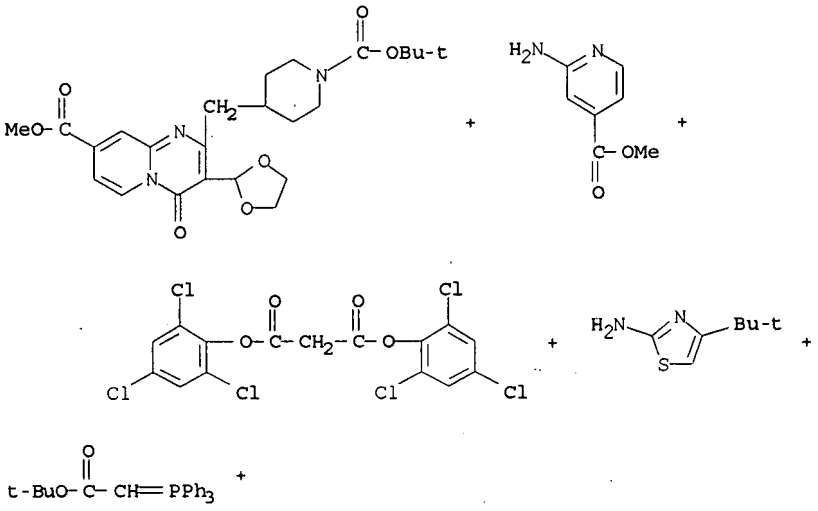
RX(420) OF 531 - 9 STEPS



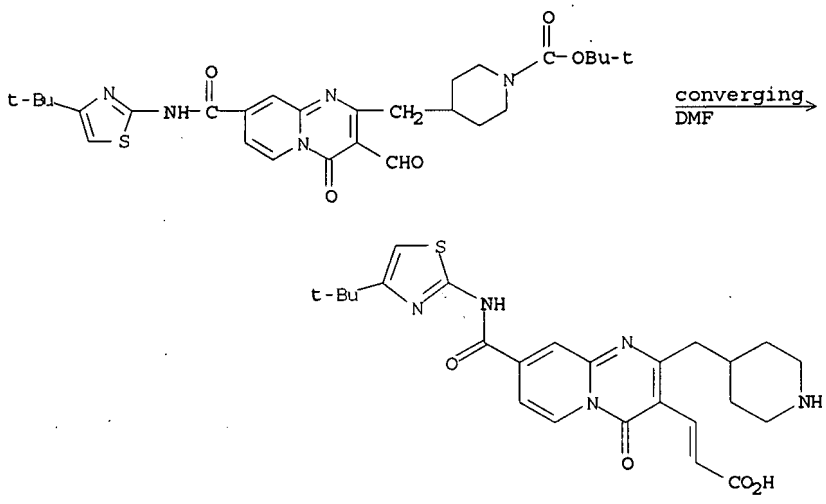
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 2 hours, reflux
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(421) OF 531 - 8 STEPS



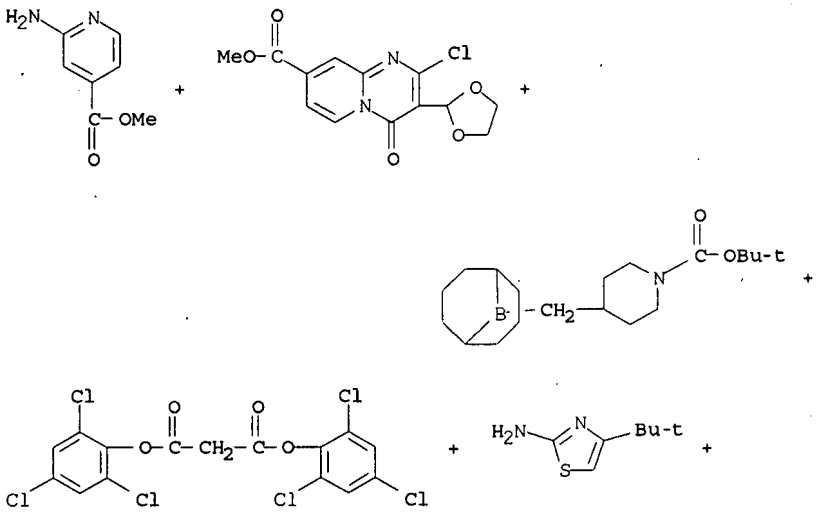
RX(421) OF 531 - 8 STEPS



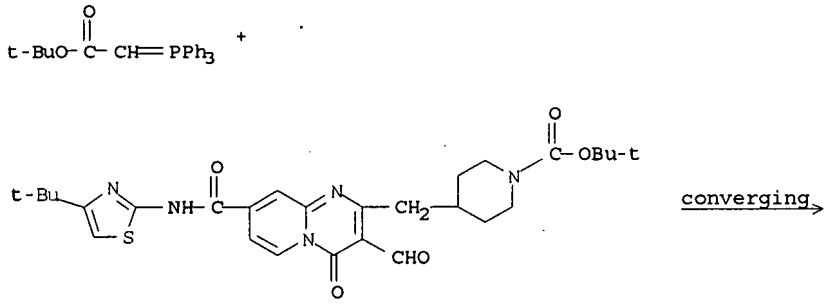
65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6.1) 30 minutes, room temperature
STEP(6.2) room temperature, pH 4
STEP(7) 12.5 hours, room temperature
STEP(8) 1 hour, 0 deg C

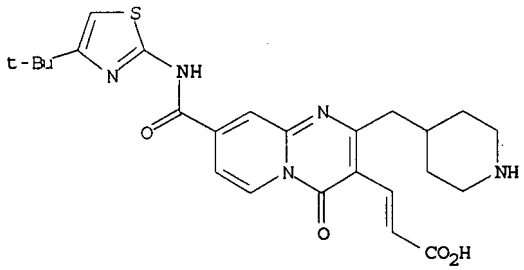
RX(422) OF 531 - 9 STEPS



RX(422) OF 531 - 9 STEPS



RX(422) OF 531 - 9 STEPS

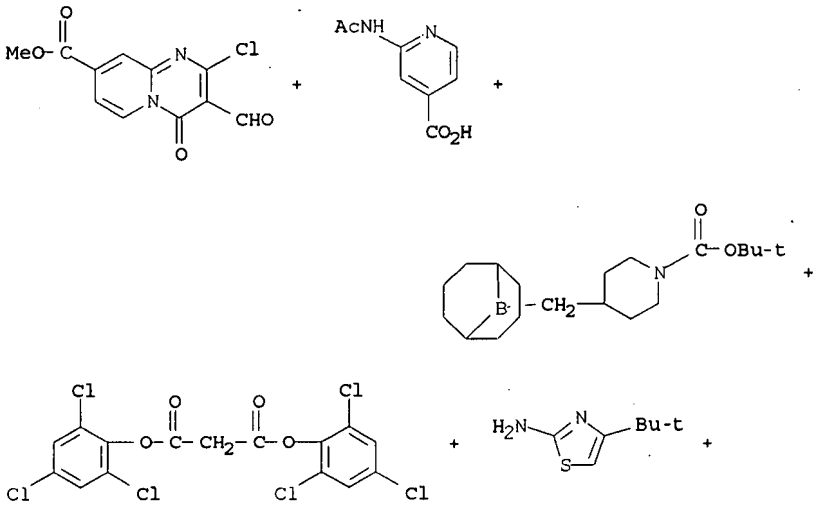


65%

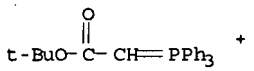
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

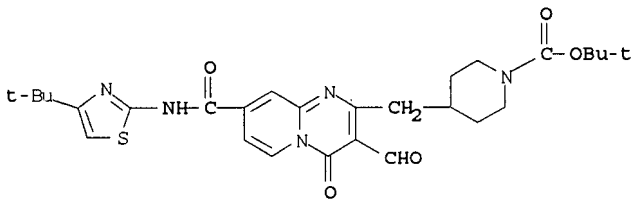
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(427) OF 531 - 10 STEPS



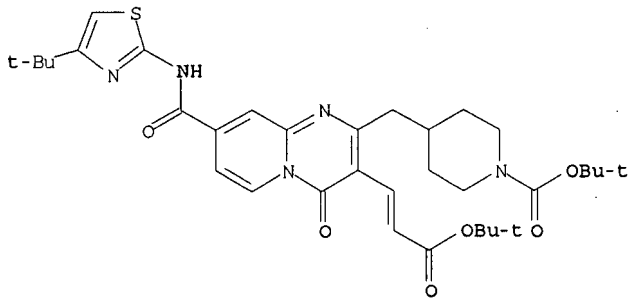
RX(427) OF 531 - 10 STEPS





converging
MeOH, (CH2OH)2

RX(427) OF 531 - 10 STEPS

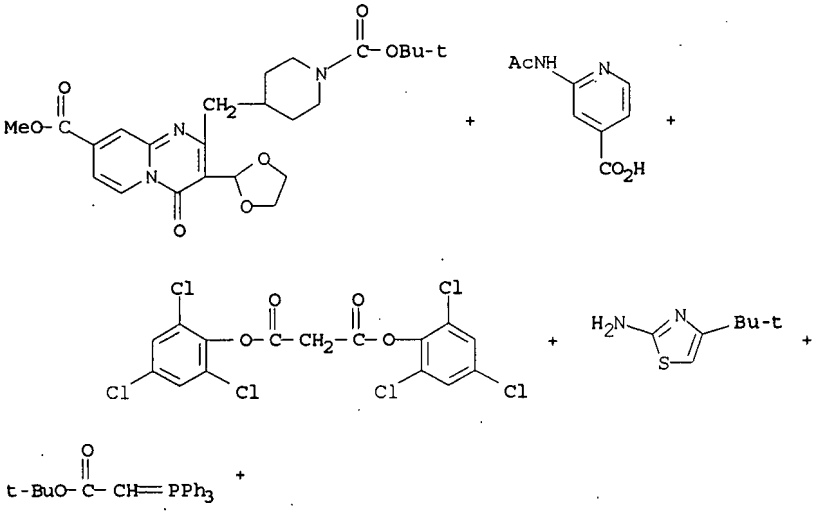


87%

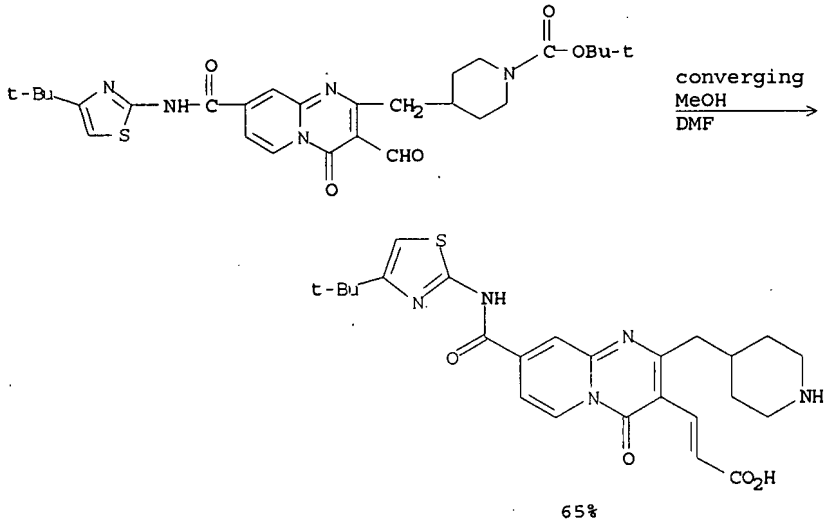
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 2 hours, reflux
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(428) OF 531 - 9 STEPS



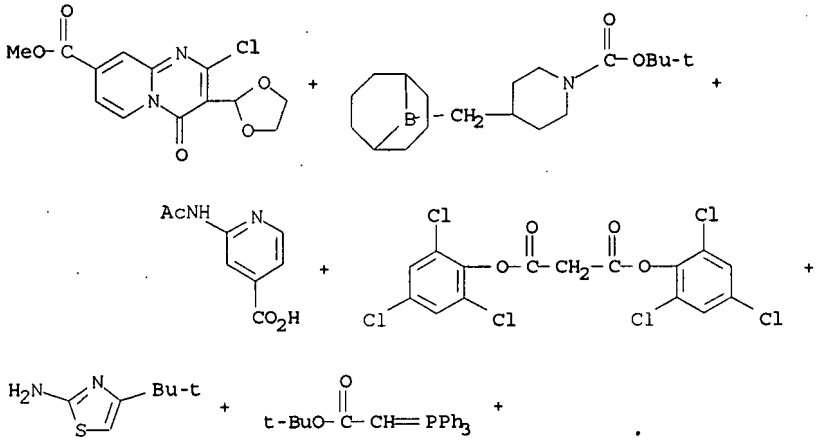
RX(428) OF 531 - 9 STEPS



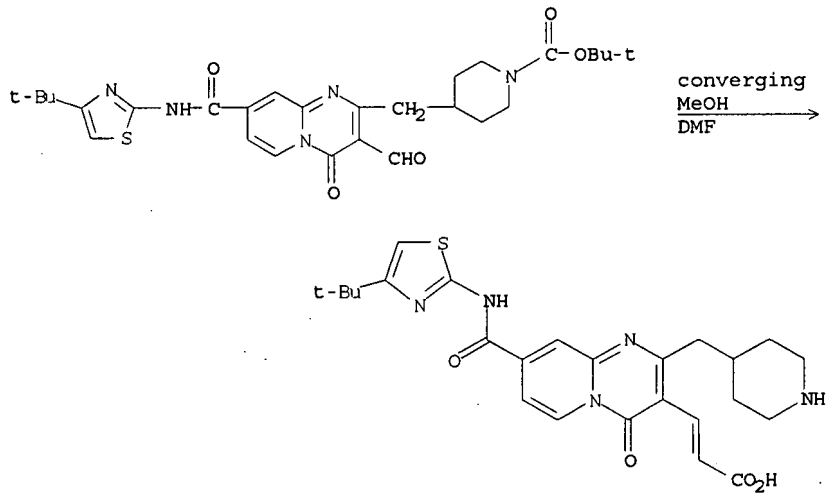
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(429) OF 531 - 10 STEPS



RX(429) OF 531 - 10 STEPS

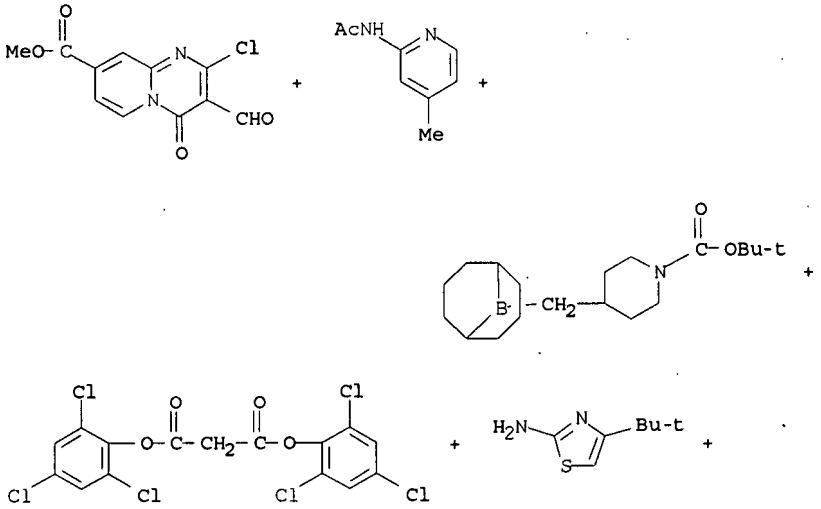


65%

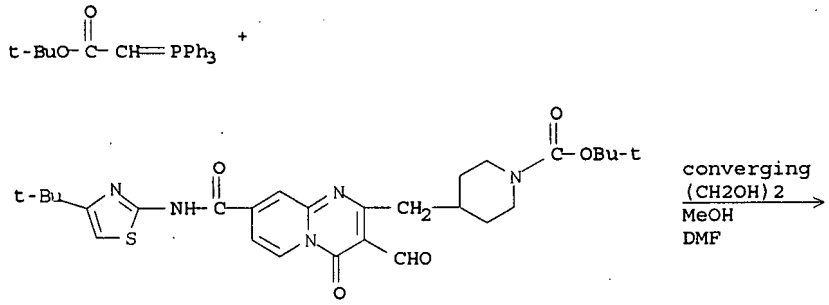
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

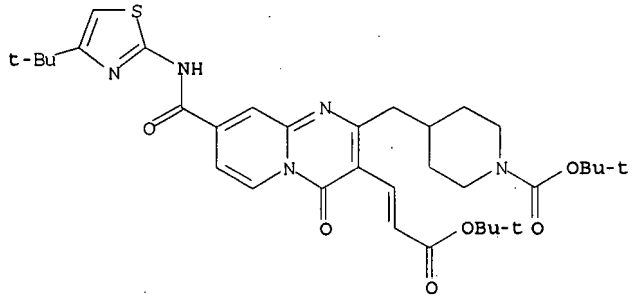
RX(434) OF 531 - 11 STEPS



RX(434) OF 531 - 11 STEPS



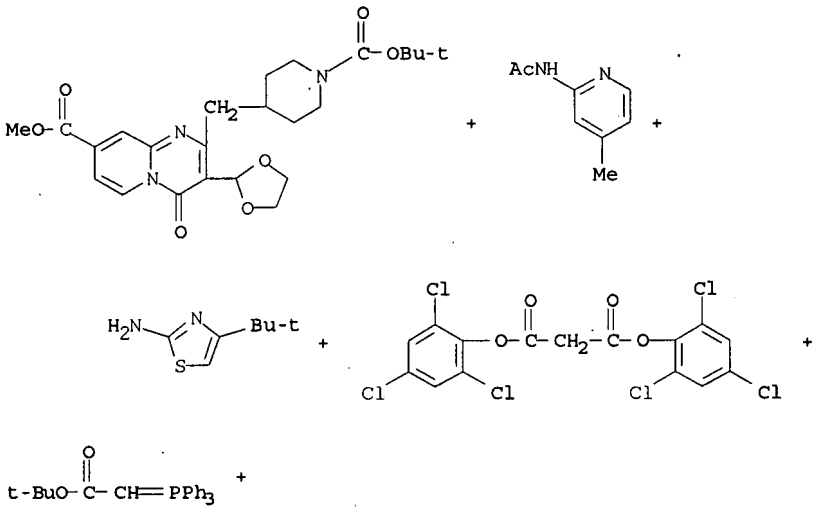
RX(434) OF 531 - 11 STEPS



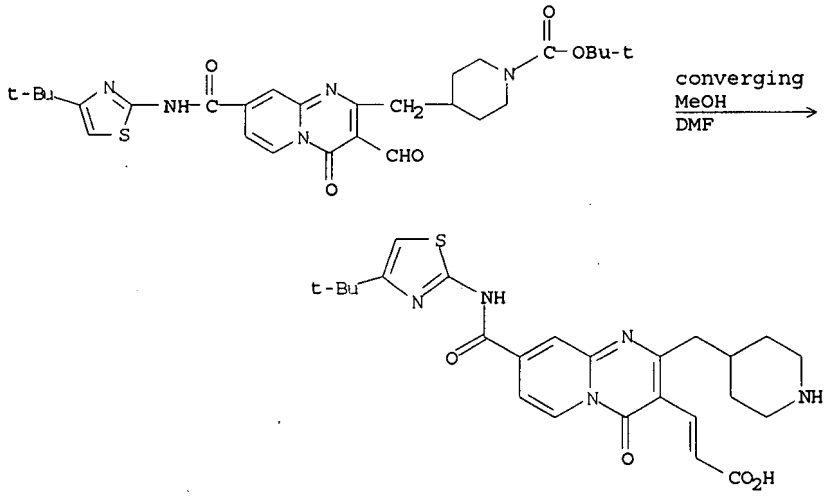
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 2 hours, reflux
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

RX(435) OF 531 - 10 STEPS



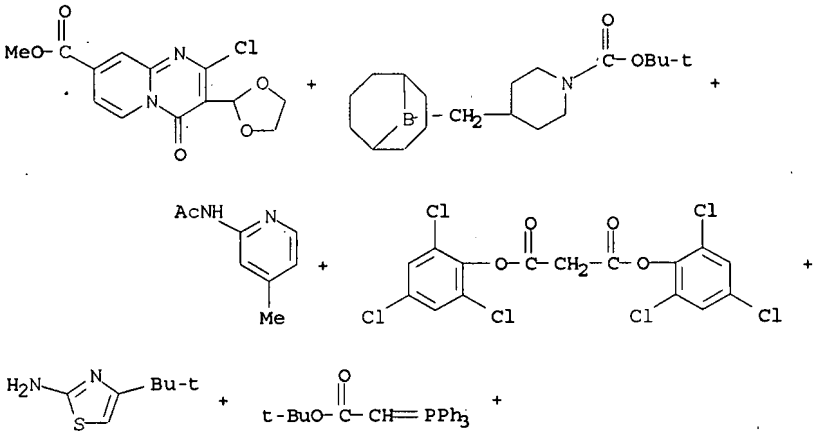
RX(435) OF 531 - 10 STEPS



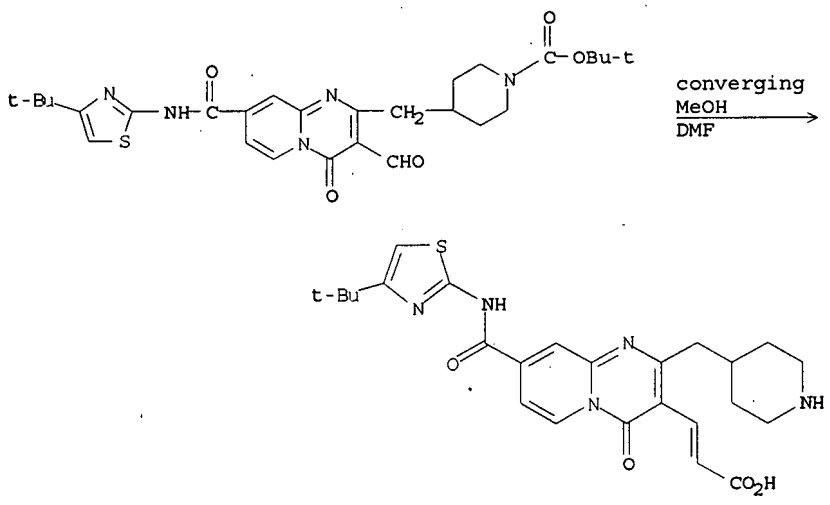
65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(436) OF 531 - 11 STEPS



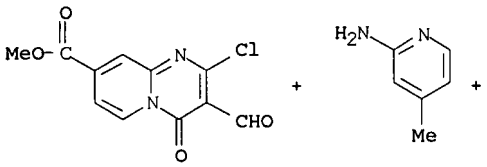
RX(436) OF 531 - 11 STEPS



65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

RX(441) OF 531 - 12 STEPS



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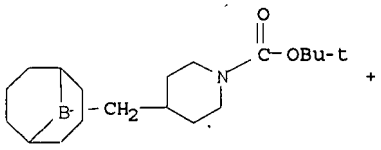
+


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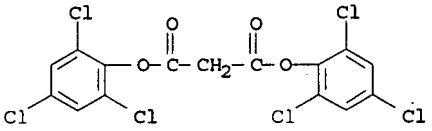

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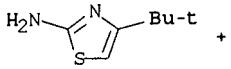

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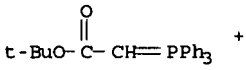
RX(441) OF 531 - 12 STEPS



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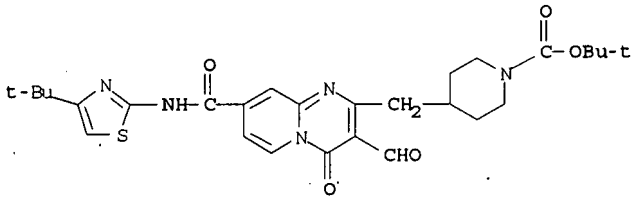
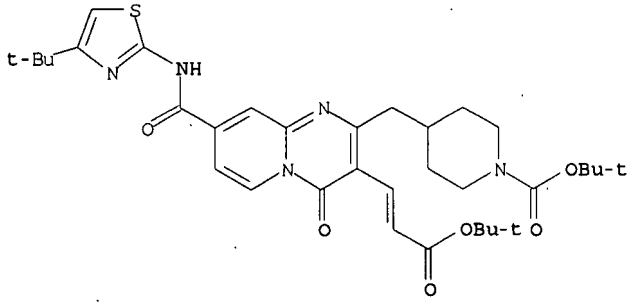


converging
Ac2O, (CH2OH)2
MeOH
DMF

RX(441) OF 531 - 12 STEPS

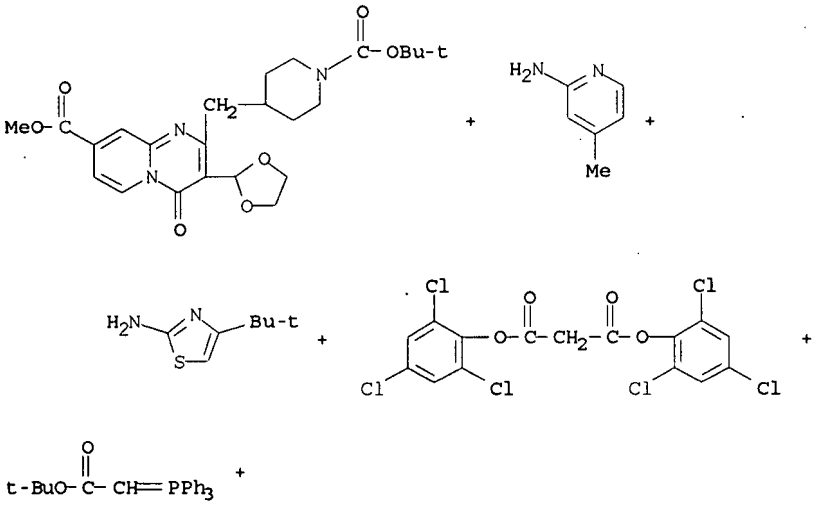


87%

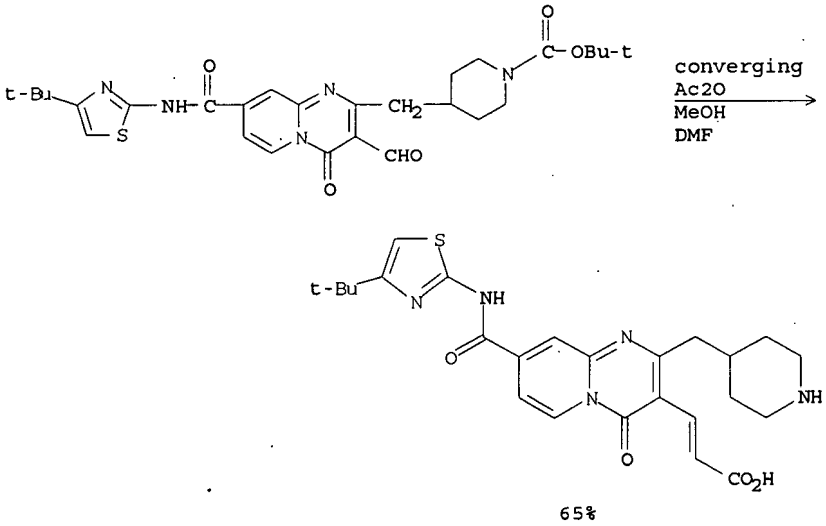
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 2 hours, reflux
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

RX(442) OF 531 - 11 STEPS



RX(442) OF 531 - 11 STEPS

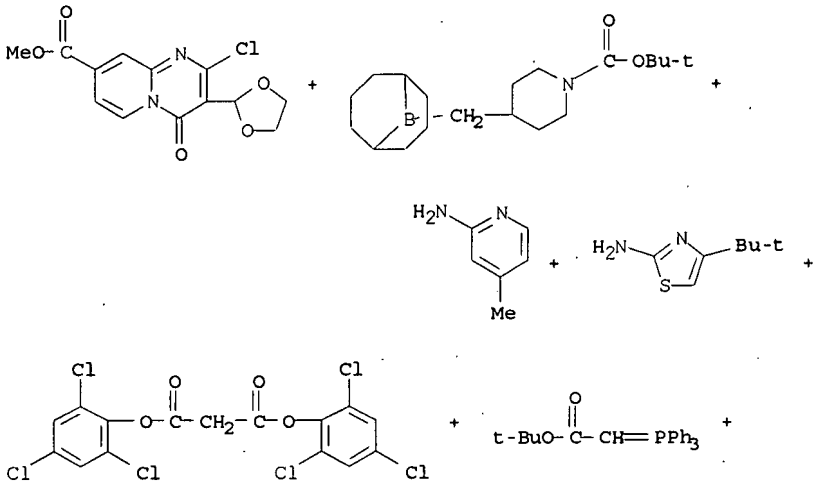


65%

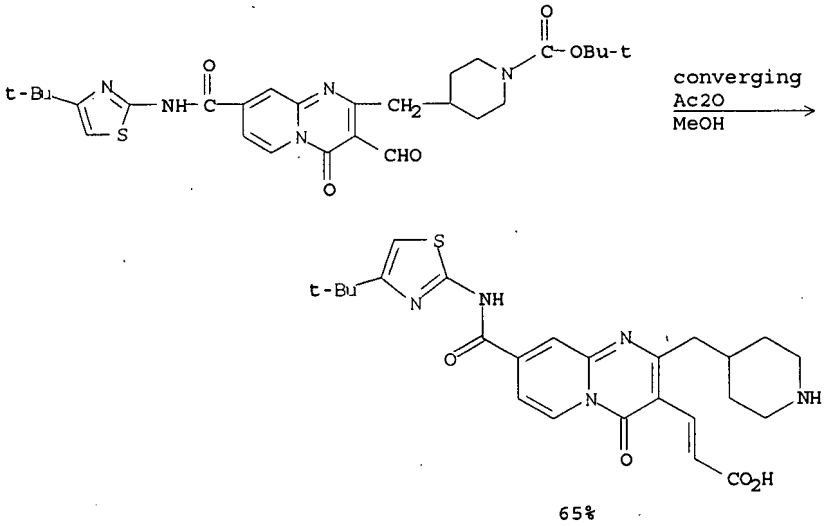
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

RX(443) OF 531 - 12 STEPS



RX(443) OF 531 - 12 STEPS

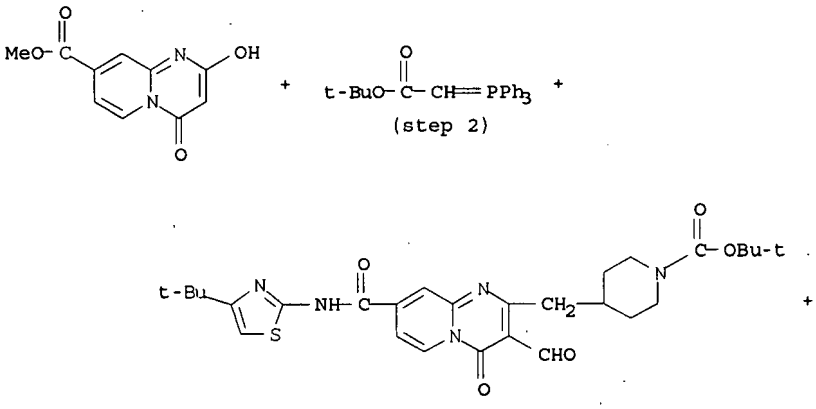


65%

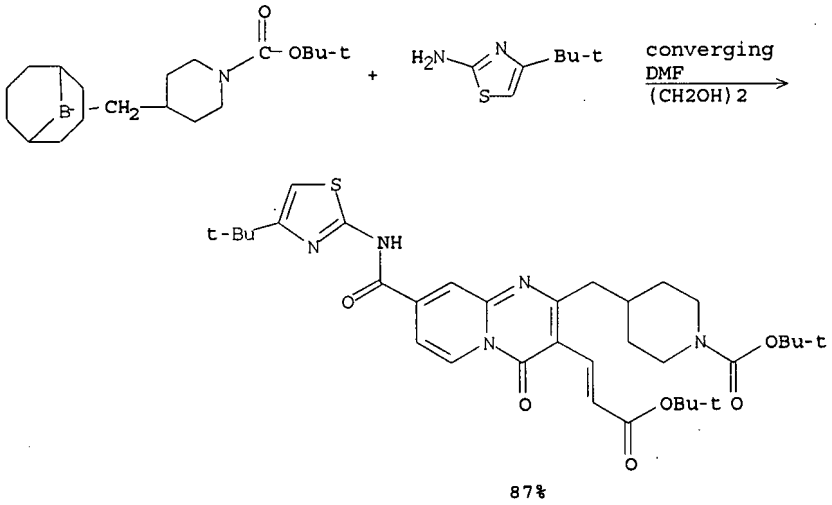
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

RX(447) OF 531 - 9 STEPS



RX(447) OF 531 - 9 STEPS

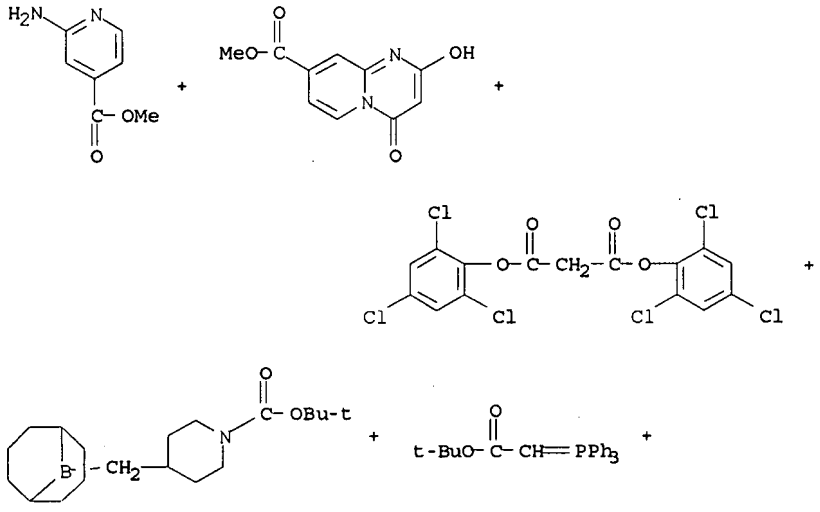


87%

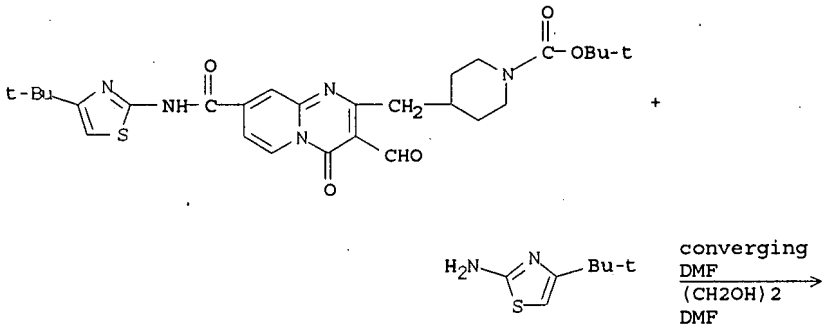
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 2 hours, reflux
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(451) OF 531 - 10 STEPS

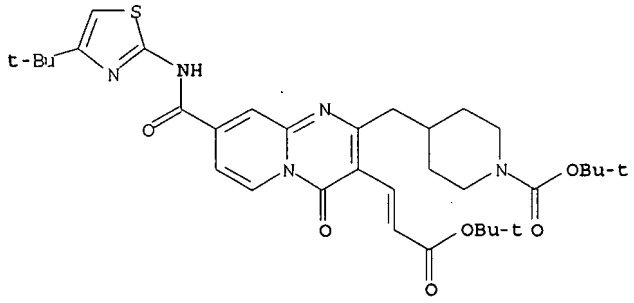


RX(451) OF 531 - 10 STEPS



converging
DMF
(CH2OH)2
DMF

RX(451) OF 531 - 10 STEPS

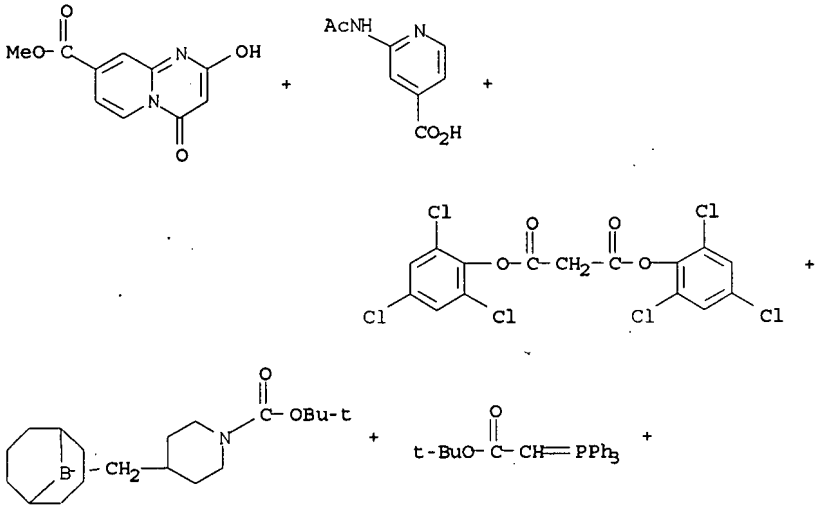


87%

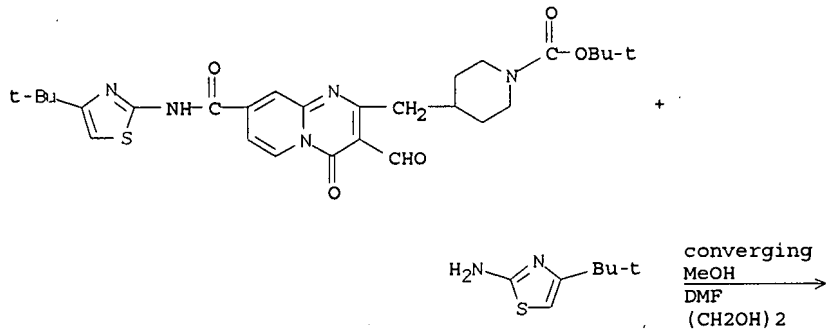
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 2 hours, reflux
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(456) OF 531 - 11 STEPS

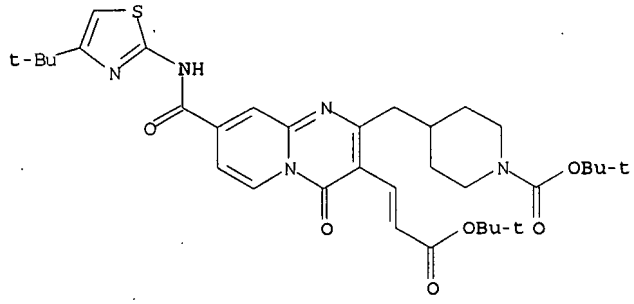


RX(456) OF 531 - 11 STEPS



converging
MeOH
DMF
(CH2OH)2

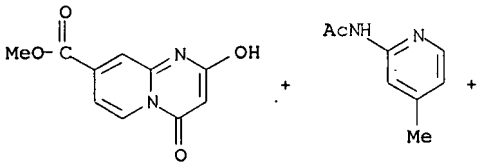
RX(456) OF 531 - 11 STEPS

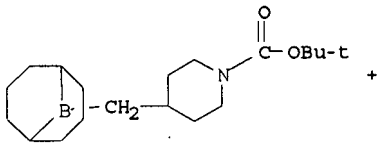


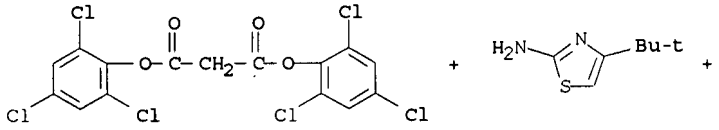
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6.1) 40 minutes, 0 deg C
STEP(6.2) 1 hour, 80 deg C
STEP(7) 2 hours, reflux
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

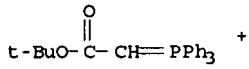
RX(461) OF 531 - 12 STEPS

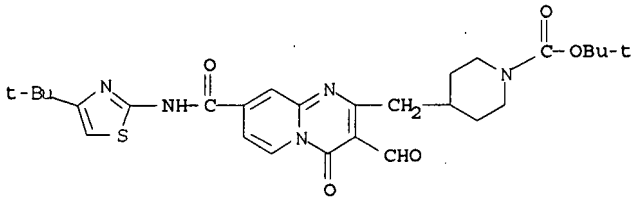






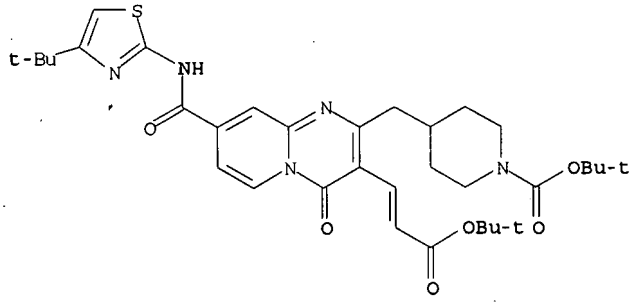
RX(461) OF 531 - 12 STEPS





converging
DMF
MeOH, (CH2OH)2

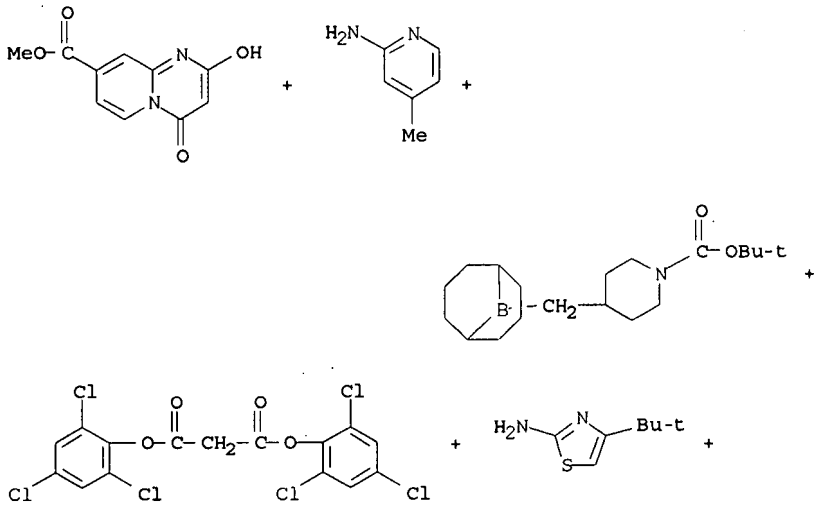
RX(461) OF 531 - 12 STEPS



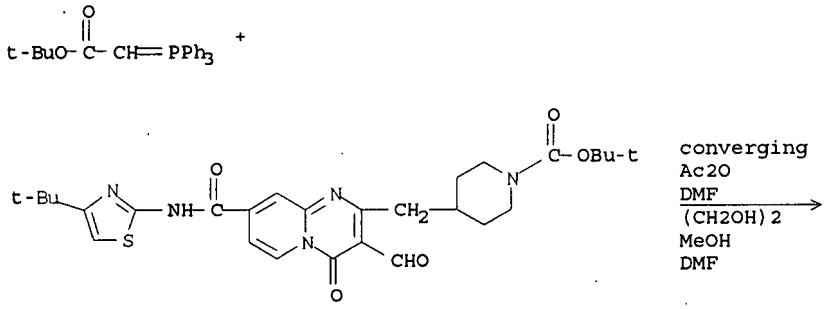
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7.1) 40 minutes, 0 deg C
STEP(7.2) 1 hour, 80 deg C
STEP(8) 2 hours, reflux
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

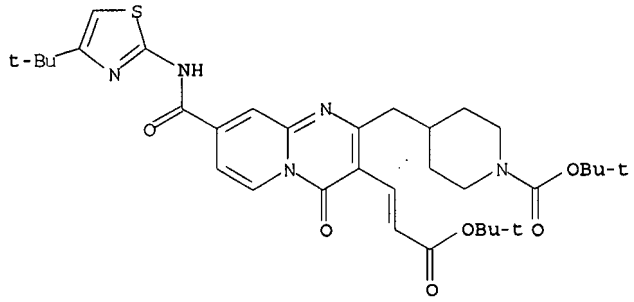
RX(466) OF 531 - 13 STEPS



RX(466) OF 531 - 13 STEPS



RX(466) OF 531 - 13 STEPS

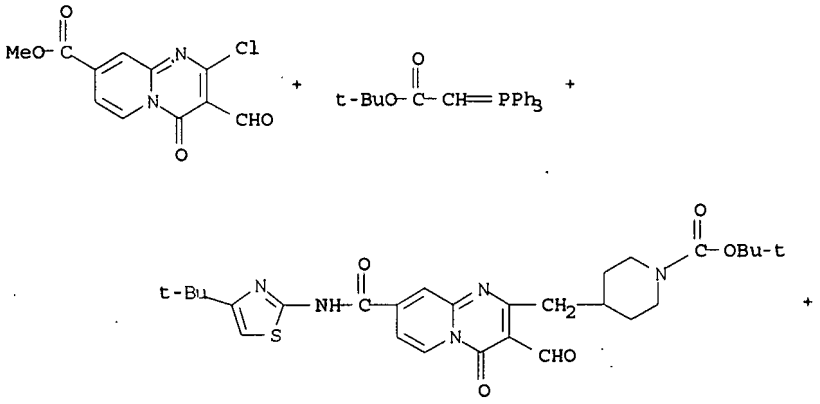


87%

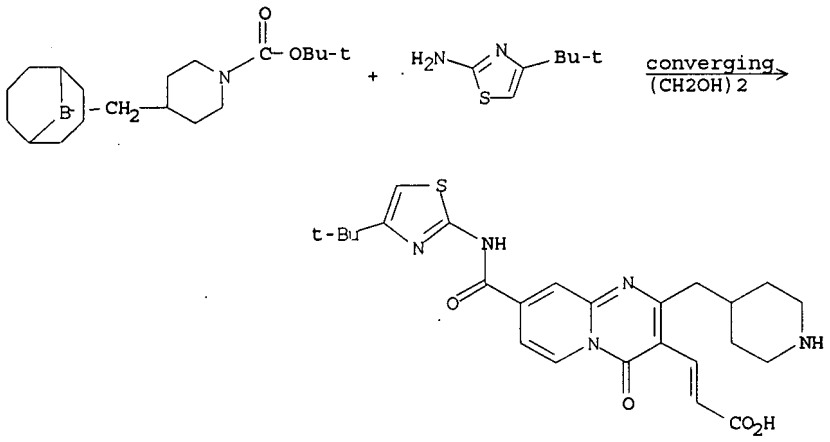
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8.1) 40 minutes, 0 deg C
STEP(8.2) 1 hour, 80 deg C
STEP(9) 2 hours, reflux
STEP(10.1) 1 hour, reflux
STEP(10.2) room temperature; 4 hours, 60 deg C
STEP(11.1) 30 minutes, room temperature
STEP(11.2) room temperature, pH 4
STEP(12) 12.5 hours, room temperature
STEP(13) 1 hour, 0 deg C

RX(468) OF 531 - 8 STEPS



RX(468) OF 531 - 8 STEPS

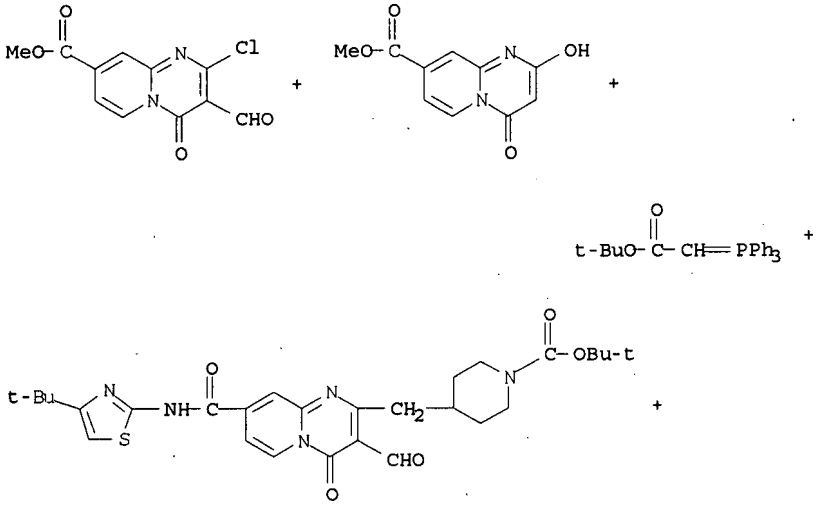


65%

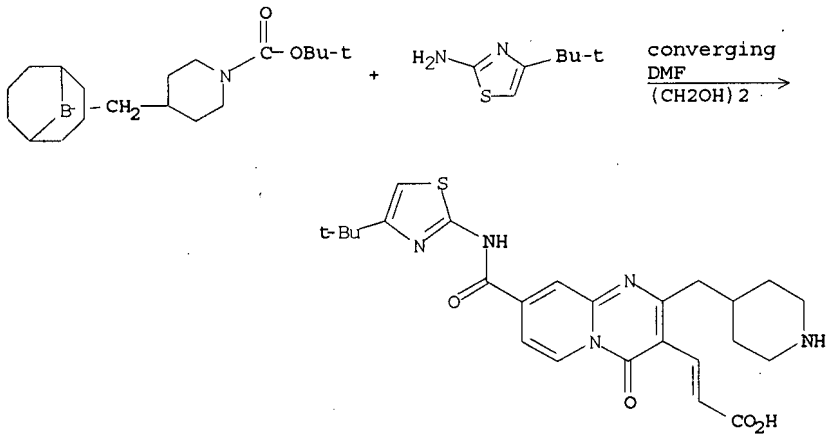
NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature
STEP(4) 2 hours, reflux
STEP(5.1) 1 hour, reflux
STEP(5.2) room temperature; 4 hours, 60 deg C
STEP(6.1) 30 minutes, room temperature
STEP(6.2) room temperature, pH 4
STEP(7) 12.5 hours, room temperature
STEP(8) 1 hour, 0 deg C

RX(469) OF 531 - 9 STEPS



RX(469) OF 531 - 9 STEPS

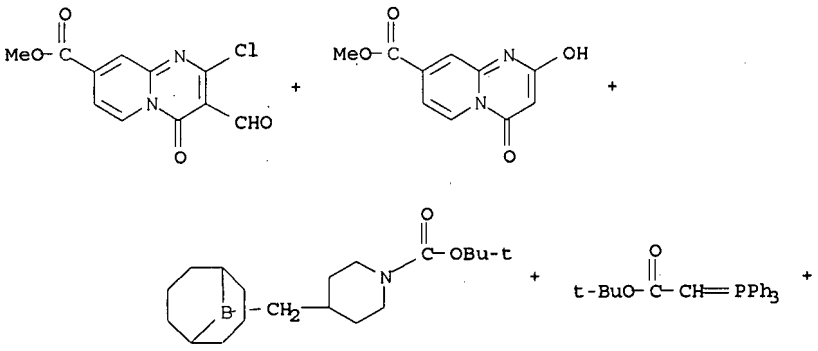


65%

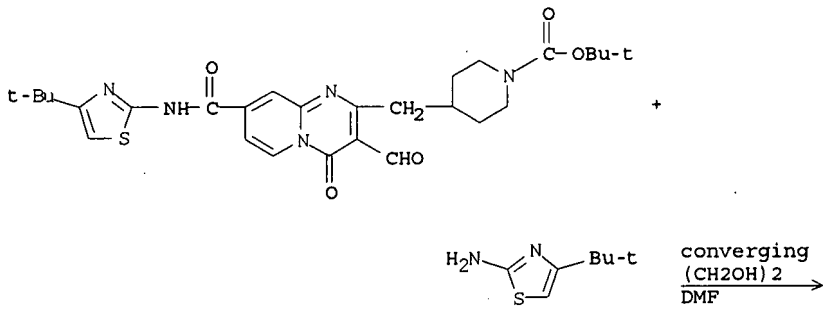
NOTE: Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) 47 hours, room temperature
STEP(2) 47 hours, room temperature
STEP(3) 30 minutes, room temperature
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 2 hours, reflux
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(470) OF 531 - 9 STEPS

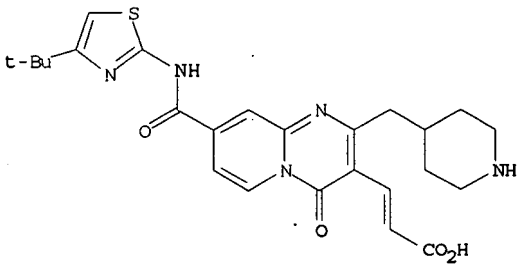


RX(470) OF 531 - 9 STEPS



converging
(CH2OH)2
DMF

RX(470) OF 531 - 9 STEPS

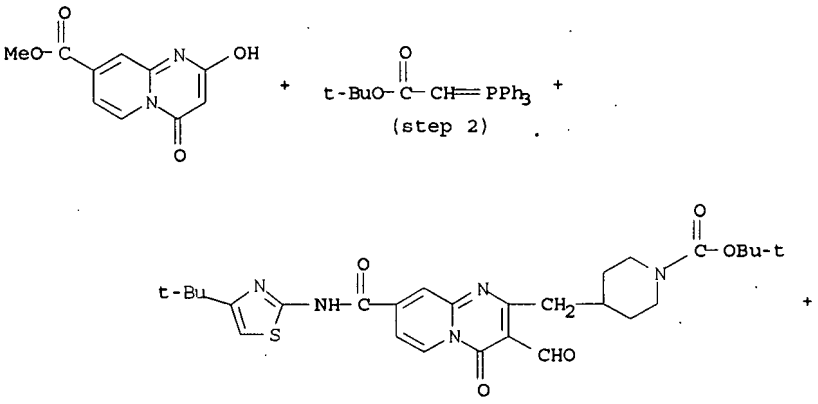


65%

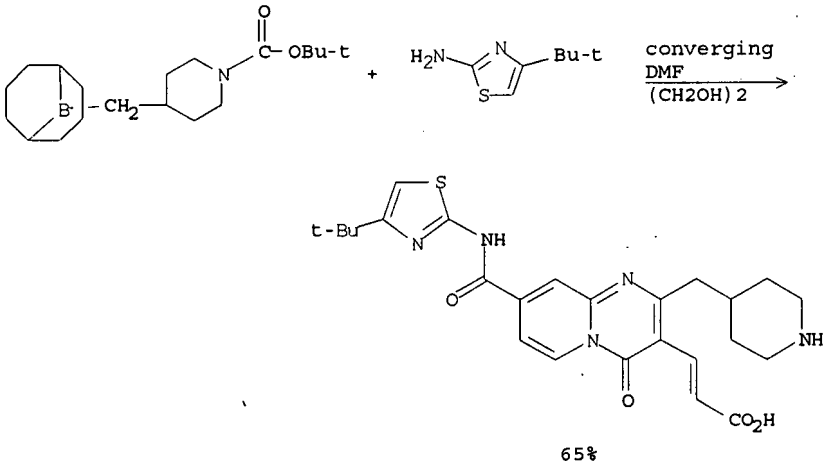
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 30 minutes, room temperature
STEP(5) 2 hours, reflux
STEP(6.1) 1 hour, reflux
STEP(6.2) room temperature; 4 hours, 60 deg C
STEP(7.1) 30 minutes, room temperature
STEP(7.2) room temperature, pH 4
STEP(8) 12.5 hours, room temperature
STEP(9) 1 hour, 0 deg C

RX(471) OF 531 - 10 STEPS



RX(471) OF 531 - 10 STEPS

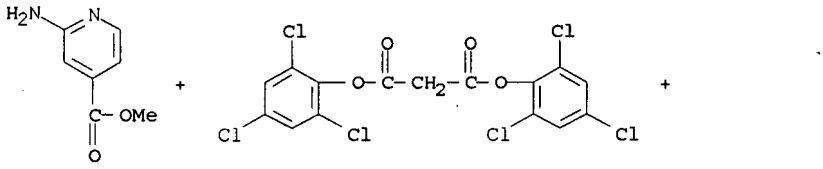


65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

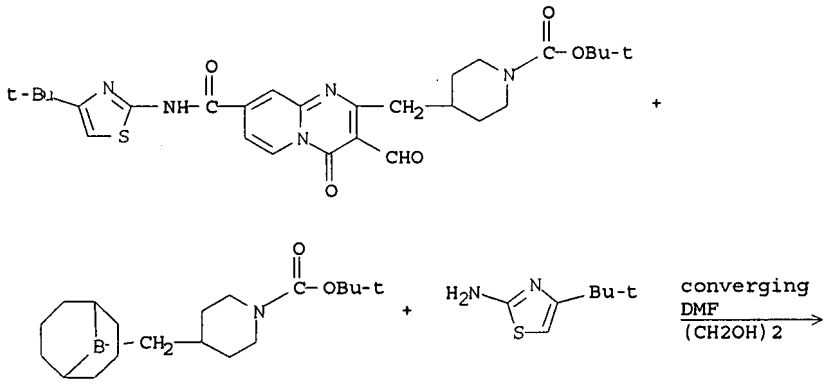
CON: STEP(1.1) 40 minutes, 0 deg C
STEP(1.2) 1 hour, 80 deg C
STEP(2) 47 hours, room temperature
STEP(3) 47 hours, room temperature
STEP(4) 30 minutes, room temperature
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 2 hours, reflux
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(472) OF 531 - 11 STEPS

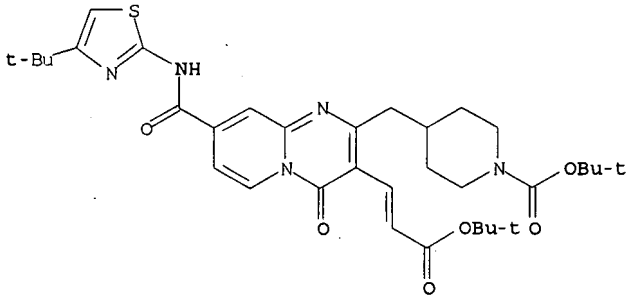


(step 3)

RX(472) OF 531 - 11 STEPS



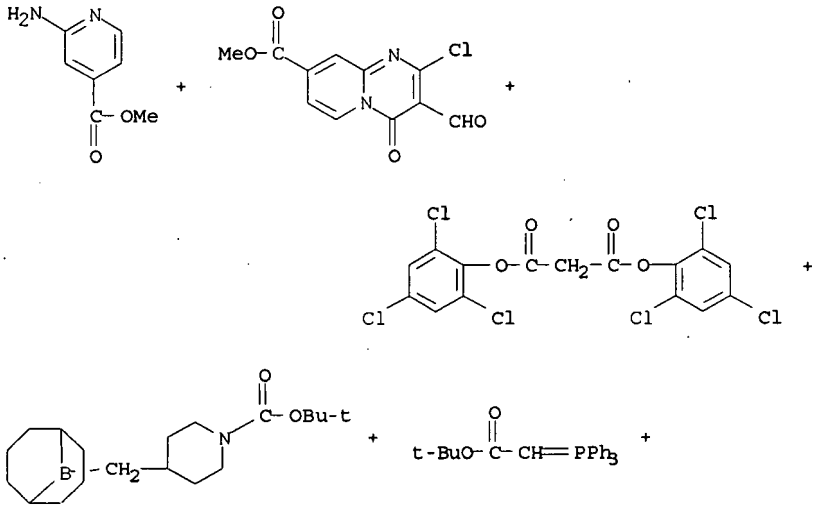
RX(472) OF 531 - 11 STEPS



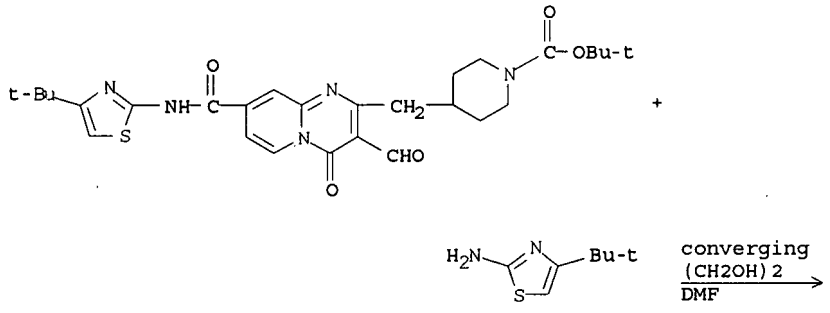
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 1 hour, reflux
STEP(6.1) 40 minutes, 0 deg C
STEP(6.2) 1 hour, 80 deg C
STEP(7) 2 hours, reflux
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

RX(473) OF 531 - 10 STEPS

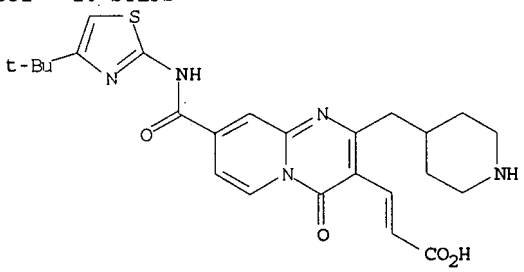


RX(473) OF 531 - 10 STEPS



converging
(CH2OH)2
DMF

RX(473) OF 531 - 10 STEPS

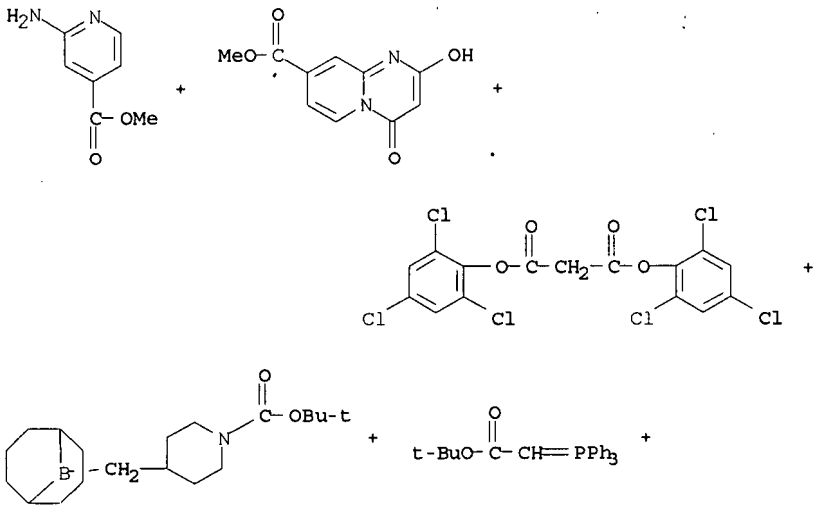


65%

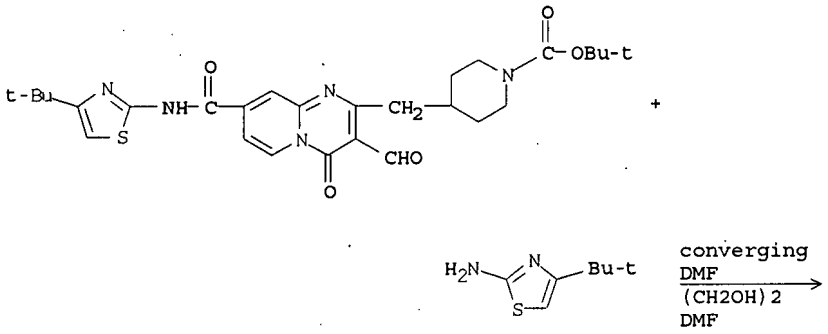
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6) 2 hours, reflux
STEP(7.1) 1 hour, reflux
STEP(7.2) room temperature; 4 hours, 60 deg C
STEP(8.1) 30 minutes, room temperature
STEP(8.2) room temperature, pH 4
STEP(9) 12.5 hours, room temperature
STEP(10) 1 hour, 0 deg C

RX(474) OF 531 - 11 STEPS

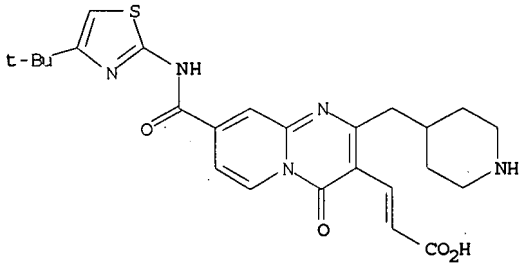


RX(474) OF 531 - 11 STEPS



converging
DMF
(CH2OH)2
DMF

RX(474) OF 531 - 11 STEPS

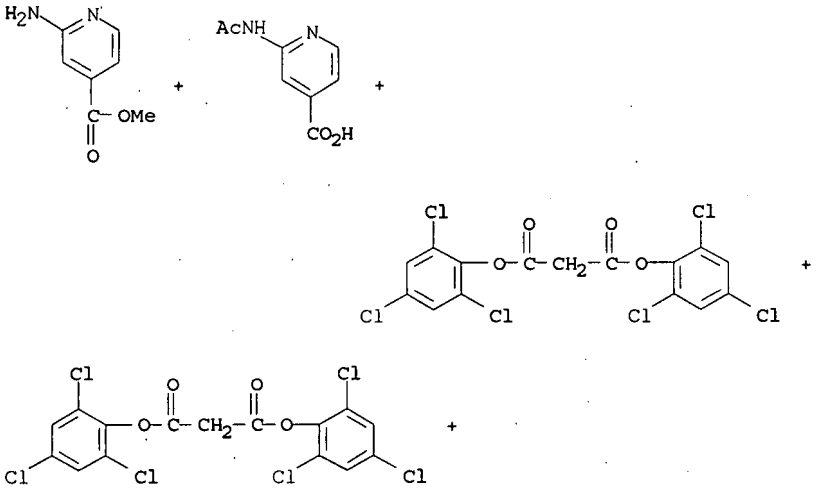


65%

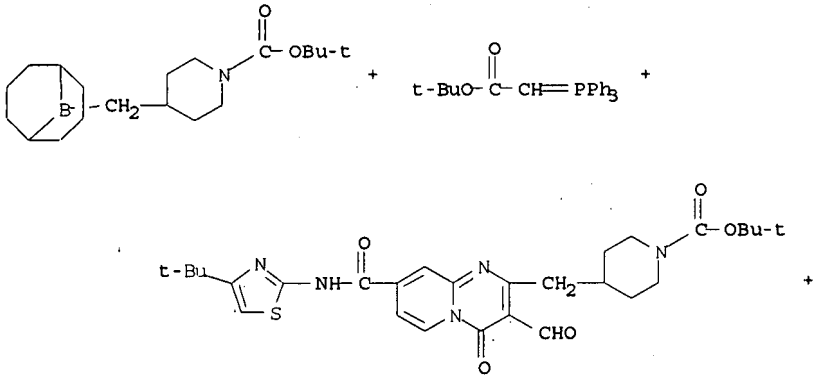
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) 1 hour, reflux
STEP(2.1) 40 minutes, 0 deg C
STEP(2.2) 1 hour, 80 deg C
STEP(3) 47 hours, room temperature
STEP(4) 47 hours, room temperature
STEP(5) 30 minutes, room temperature
STEP(6.1) 40 minutes, 0 deg C
STEP(6.2) 1 hour, 80 deg C
STEP(7) 2 hours, reflux
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

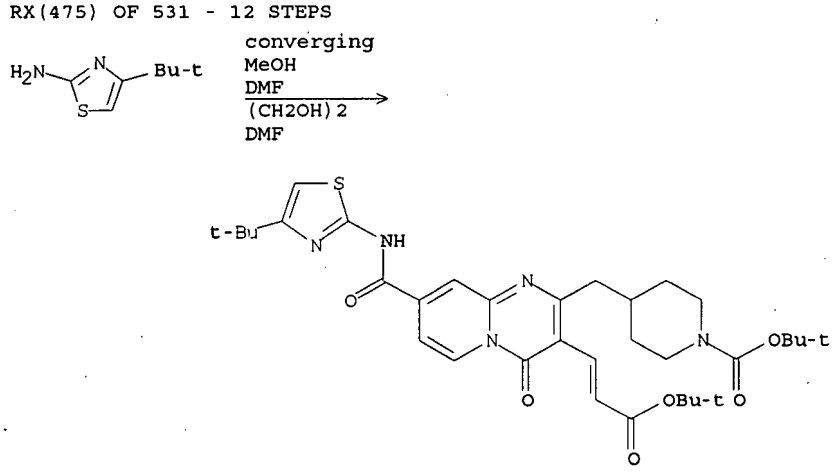
RX(475) OF 531 - 12 STEPS



RX(475) OF 531 - 12 STEPS



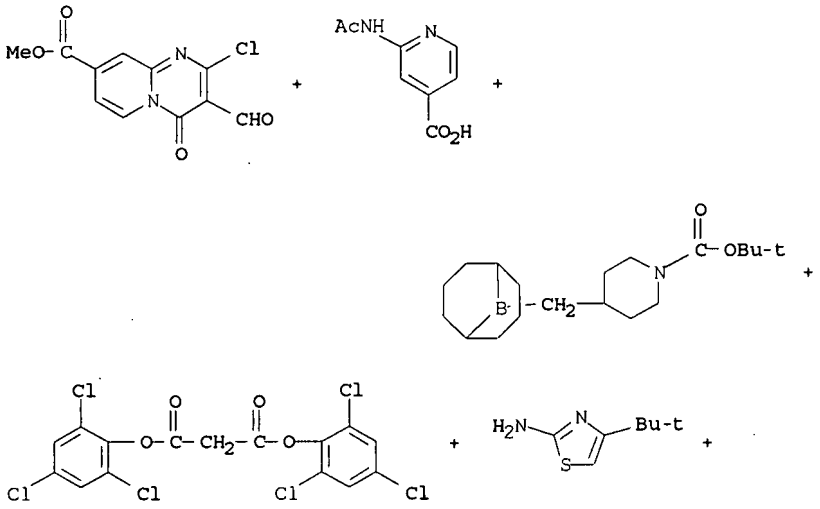
RX(475) OF 531 - 12 STEPS



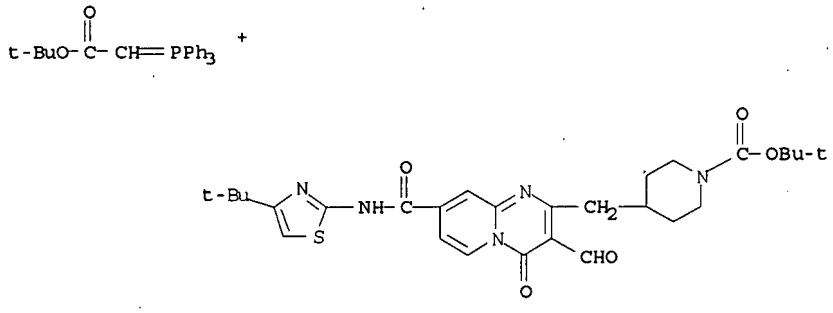
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 1 hour, reflux
STEP(7.1) 40 minutes, 0 deg C
STEP(7.2) 1 hour, 80 deg C
STEP(8) 2 hours, reflux
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

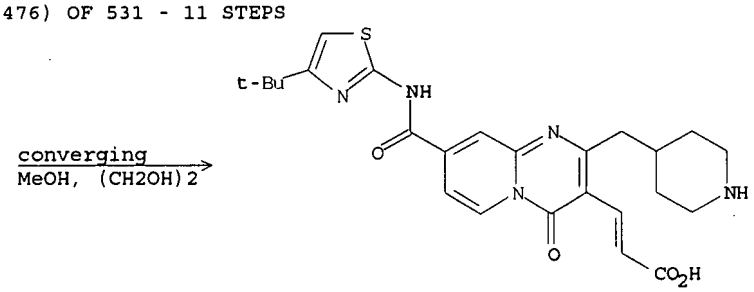
RX(476) OF 531 - 11 STEPS



RX(476) OF 531 - 11 STEPS



RX(476) OF 531 - 11 STEPS

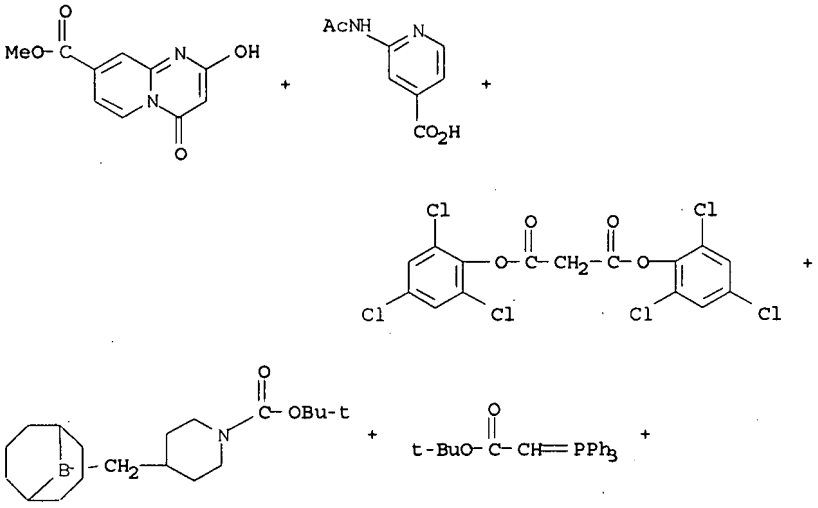


65%

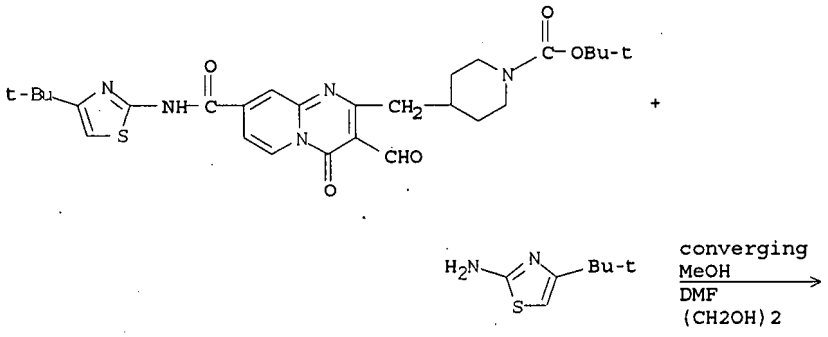
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7) 2 hours, reflux
STEP(8.1) 1 hour, reflux
STEP(8.2) room temperature; 4 hours, 60 deg C
STEP(9.1) 30 minutes, room temperature
STEP(9.2) room temperature, pH 4
STEP(10) 12.5 hours, room temperature
STEP(11) 1 hour, 0 deg C

RX(477) OF 531 - 12 STEPS

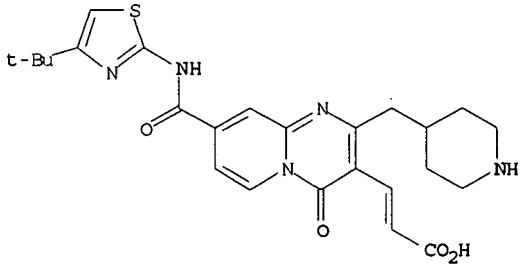


RX(477) OF 531 - 12 STEPS



converging
MeOH
DMF
(CH2OH)2

RX(477) OF 531 - 12 STEPS

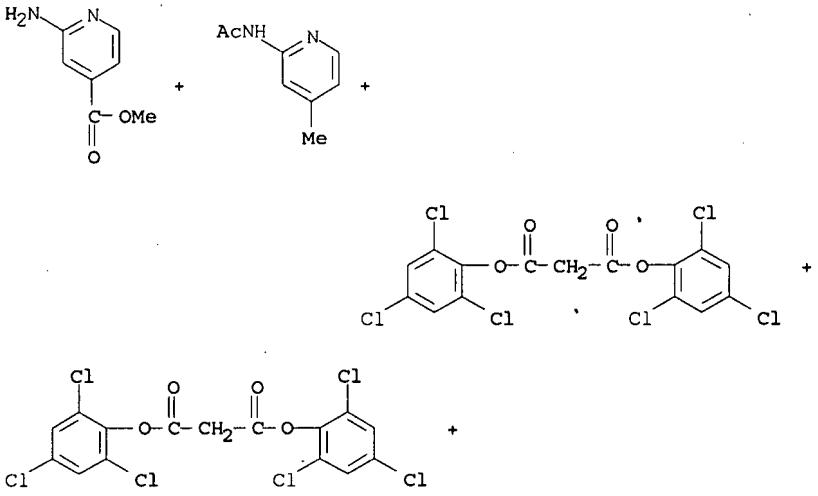


65%

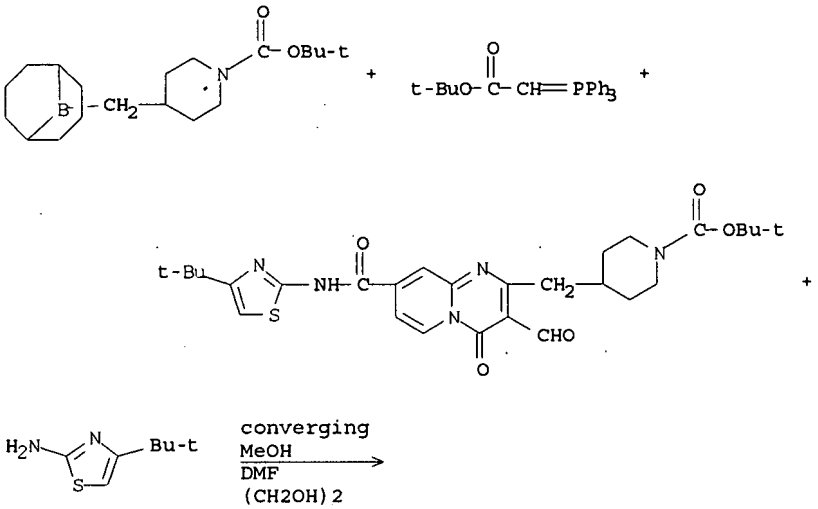
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) 1 hour, reflux
STEP(3.1) 40 minutes, 0 deg C
STEP(3.2) 1 hour, 80 deg C
STEP(4) 47 hours, room temperature
STEP(5) 47 hours, room temperature
STEP(6) 30 minutes, room temperature
STEP(7.1) 40 minutes, 0 deg C
STEP(7.2) 1 hour, 80 deg C
STEP(8) 2 hours, reflux
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

RX(478) OF 531 - 13 STEPS

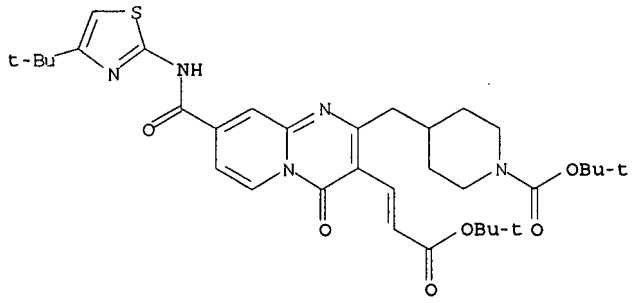


RX(478) OF 531 - 13 STEPS



converging
MeOH
DMF
(CH2OH)2

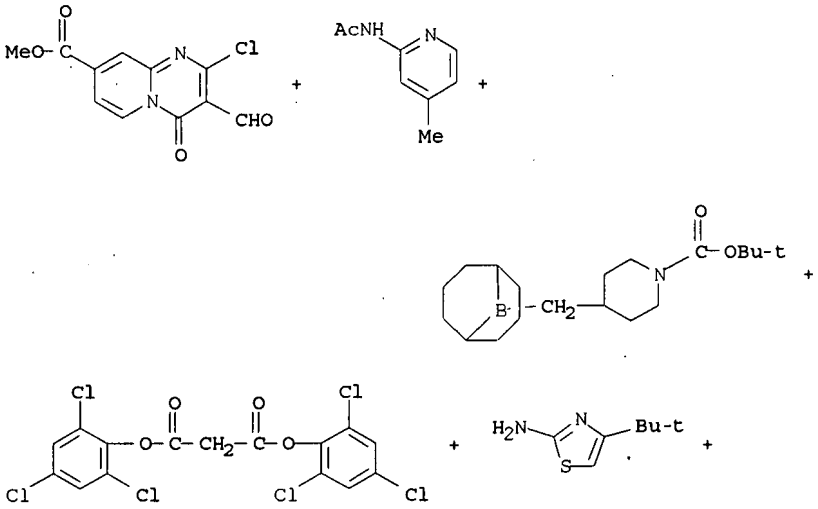
RX(478) OF 531 - 13 STEPS



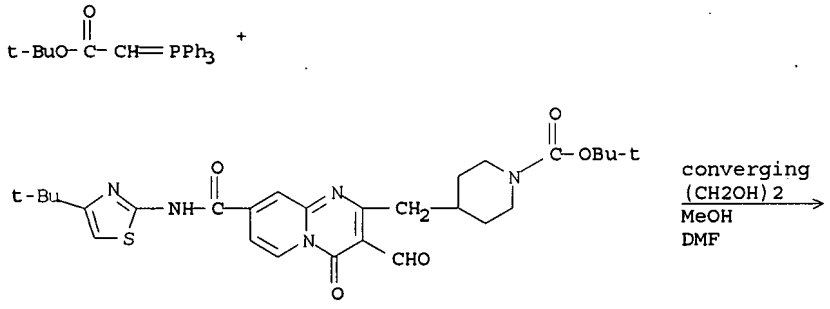
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 1 hour, reflux
STEP(8.1) 40 minutes, 0 deg C
STEP(8.2) 1 hour, 80 deg C
STEP(9) 2 hours, reflux
STEP(10.1) 1 hour, reflux
STEP(10.2) room temperature; 4 hours, 60 deg C
STEP(11.1) 30 minutes, room temperature
STEP(11.2) room temperature, pH 4
STEP(12) 12.5 hours, room temperature
STEP(13) 1 hour, 0 deg C

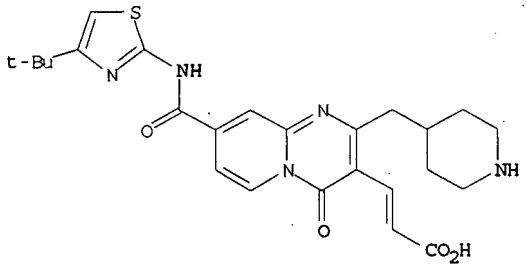
RX(479) OF 531 - 12 STEPS



RX(479) OF 531 - 12 STEPS



RX(479) OF 531 - 12 STEPS

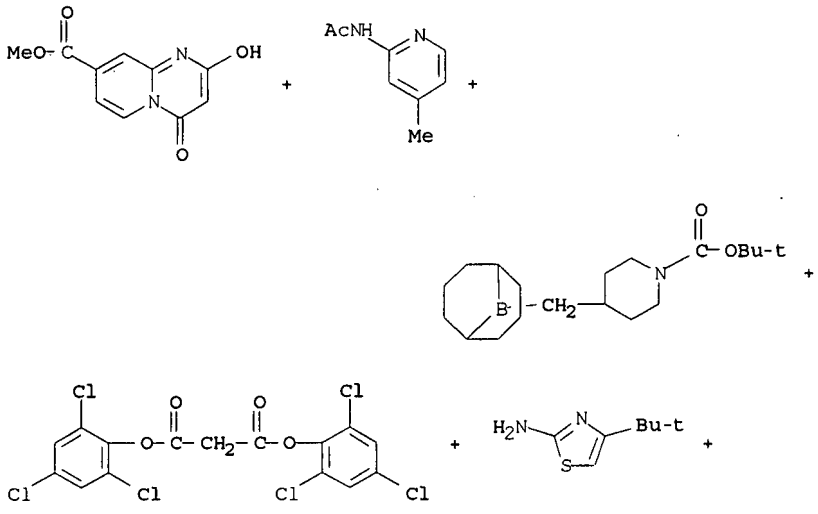


65%

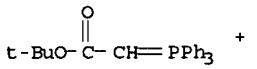
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

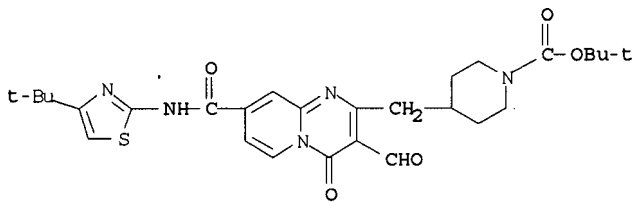
CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8) 2 hours, reflux
STEP(9.1) 1 hour, reflux
STEP(9.2) room temperature; 4 hours, 60 deg C
STEP(10.1) 30 minutes, room temperature
STEP(10.2) room temperature, pH 4
STEP(11) 12.5 hours, room temperature
STEP(12) 1 hour, 0 deg C

RX(480) OF 531 - 13 STEPS



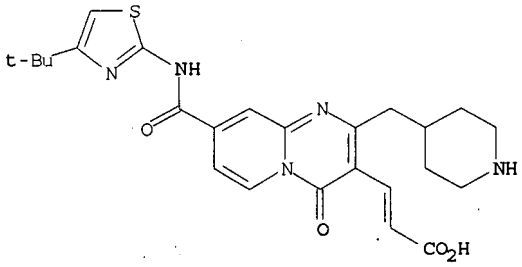
RX(480) OF 531 - 13 STEPS





RX(480) OF 531 - 13 STEPS

converging
DMF
MeOH, (CH2OH)2

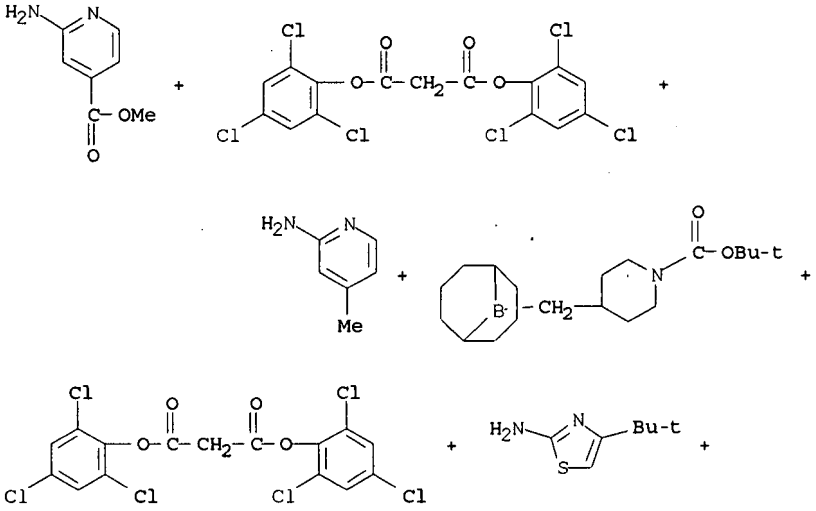


65%

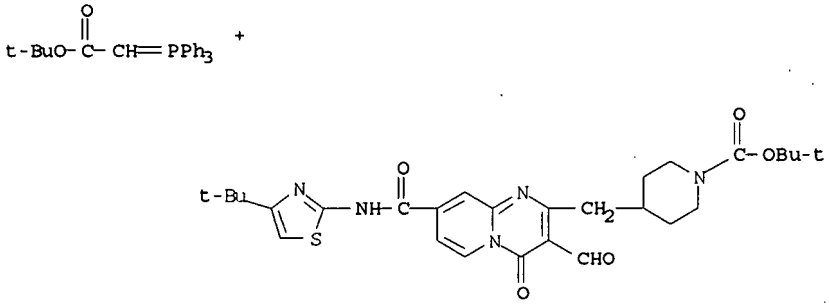
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8.1) 40 minutes, 0 deg C
STEP(8.2) 1 hour, 80 deg C
STEP(9) 2 hours, reflux
STEP(10.1) 1 hour, reflux
STEP(10.2) room temperature; 4 hours, 60 deg C
STEP(11.1) 30 minutes, room temperature
STEP(11.2) room temperature, pH 4
STEP(12) 12.5 hours, room temperature
STEP(13) 1 hour, 0 deg C

RX(481) OF 531 - 14 STEPS

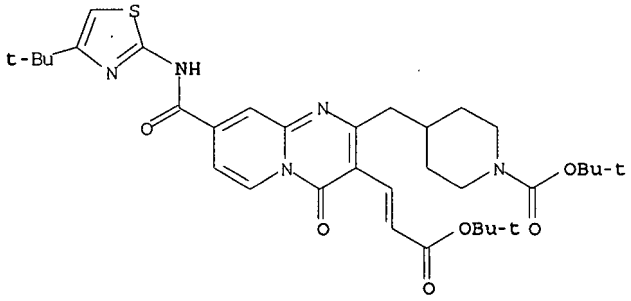


RX(481) OF 531 - 14 STEPS



converging
Ac2O
DMF
MeOH, (CH2OH)2

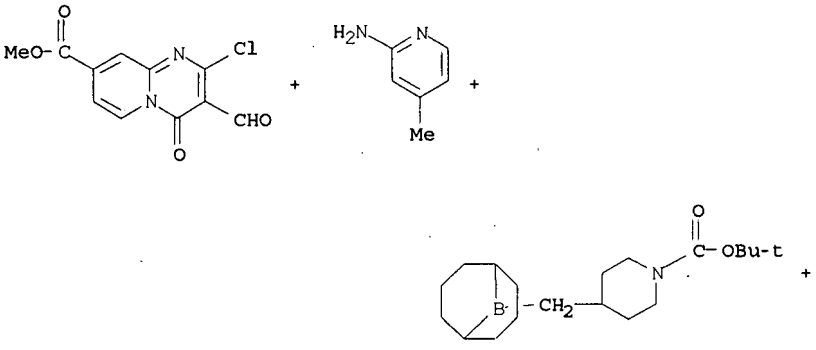
RX(481) OF 531 - 14 STEPS



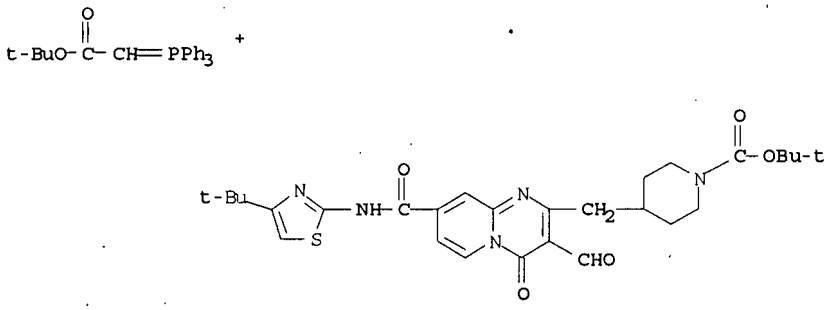
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 1 hour, reflux
STEP(9.1) 40 minutes, 0 deg C
STEP(9.2) 1 hour, 80 deg C
STEP(10) 2 hours, reflux
STEP(11.1) 1 hour, reflux
STEP(11.2) room temperature; 4 hours, 60 deg C
STEP(12.1) 30 minutes, room temperature
STEP(12.2) room temperature, pH 4
STEP(13) 12.5 hours, room temperature
STEP(14) 1 hour, 0 deg C

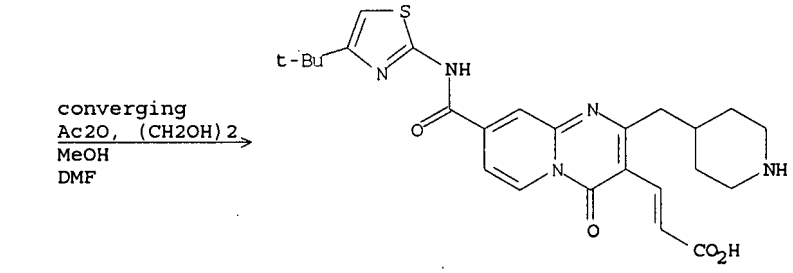
RX(482) OF 531 - 13 STEPS



RX(482) OF 531 - 13 STEPS



RX(482) OF 531 - 13 STEPS

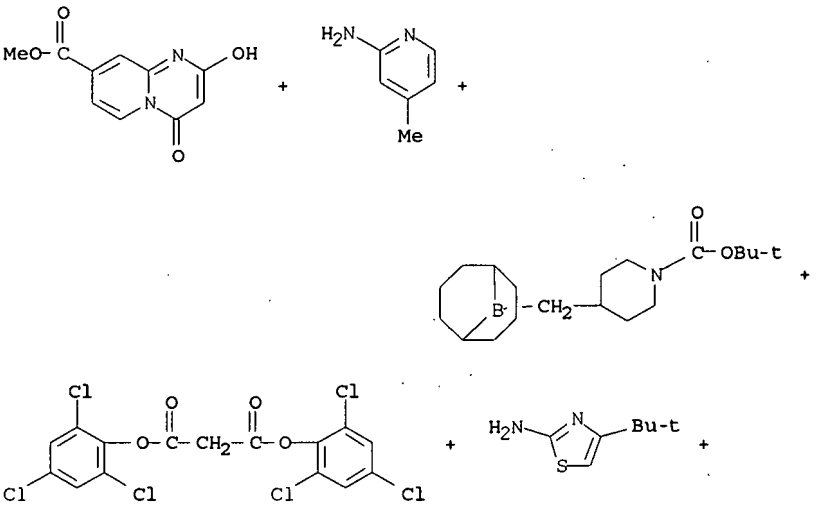


65%

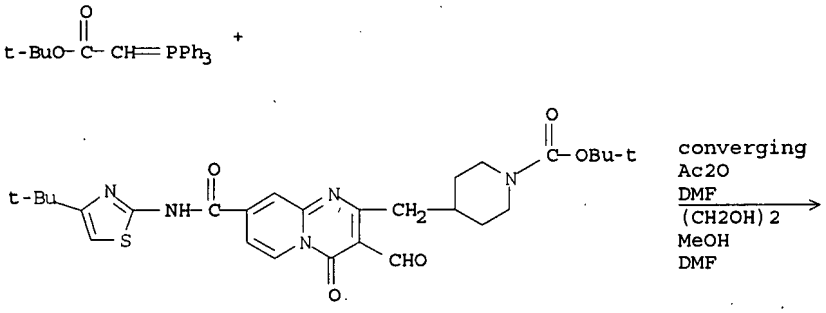
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9) 2 hours, reflux
STEP(10.1) 1 hour, reflux
STEP(10.2) room temperature; 4 hours, 60 deg C
STEP(11.1) 30 minutes, room temperature
STEP(11.2) room temperature, pH 4
STEP(12) 12.5 hours, room temperature
STEP(13) 1 hour, 0 deg C

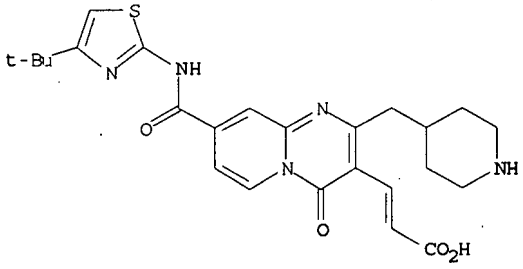
RX(483) OF 531 - 14 STEPS



RX(483) OF 531 - 14 STEPS



RX(483) OF 531 - 14 STEPS

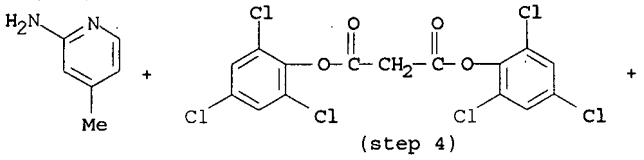


65%

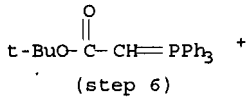
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(9.1) 40 minutes, 0 deg C
STEP(9.2) 1 hour, 80 deg C
STEP(10) 2 hours, reflux
STEP(11.1) 1 hour, reflux
STEP(11.2) room temperature; 4 hours, 60 deg C
STEP(12.1) 30 minutes, room temperature
STEP(12.2) room temperature, pH 4
STEP(13) 12.5 hours, room temperature
STEP(14) 1 hour, 0 deg C

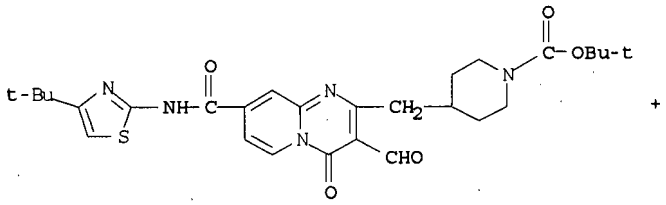
RX(527) OF 531 - 17 STEPS



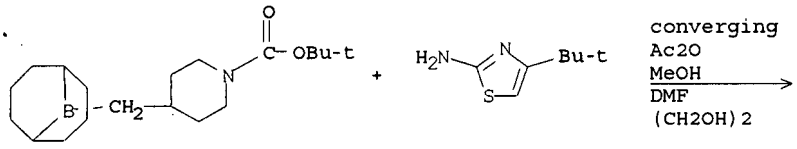
(step 4)

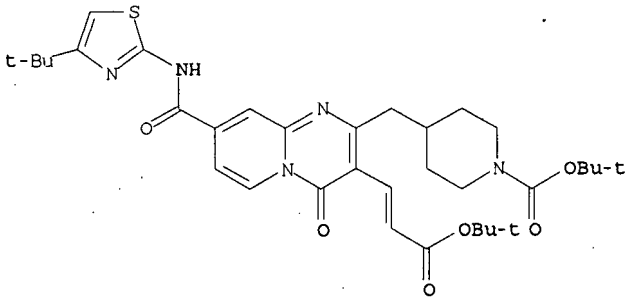


(step 6)



RX(527) OF 531 - 17 STEPS

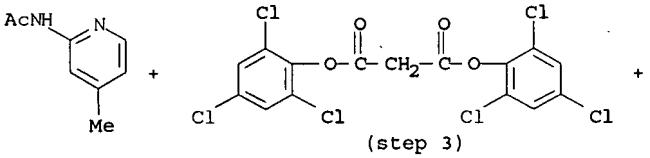




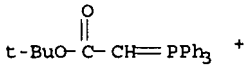
87%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(9) reflux
STEP(10) reflux
STEP(11) 1 hour, reflux
STEP(12.1) 40 minutes, 0 deg C
STEP(12.2) 1 hour, 80 deg C
STEP(13) 2 hours, reflux
STEP(14.1) 1 hour, reflux
STEP(14.2) room temperature; 4 hours, 60 deg C
STEP(15.1) 30 minutes, room temperature
STEP(15.2) room temperature, pH 4
STEP(16) 12.5 hours, room temperature
STEP(17) 1 hour, 0 deg C

RX(528) OF 531 - 16 STEPS

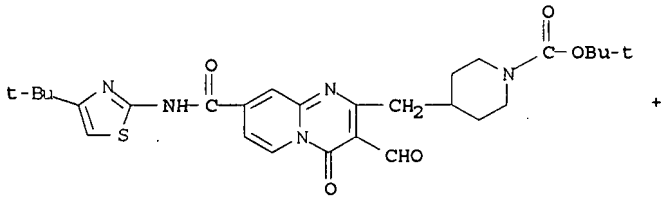


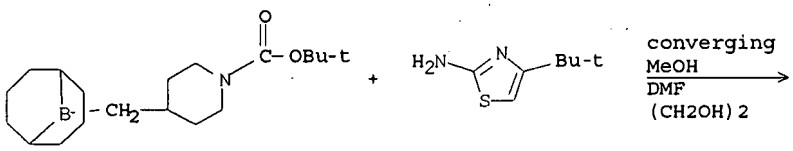
(step 3)



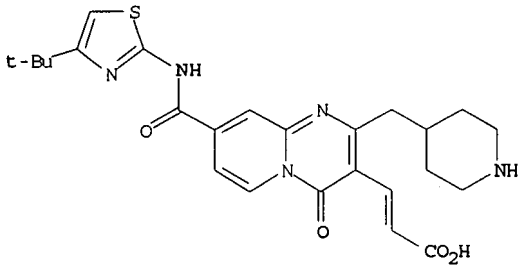
(step 5)

RX(528) OF 531 - 16 STEPS





RX(528) OF 531 - 16 STEPS

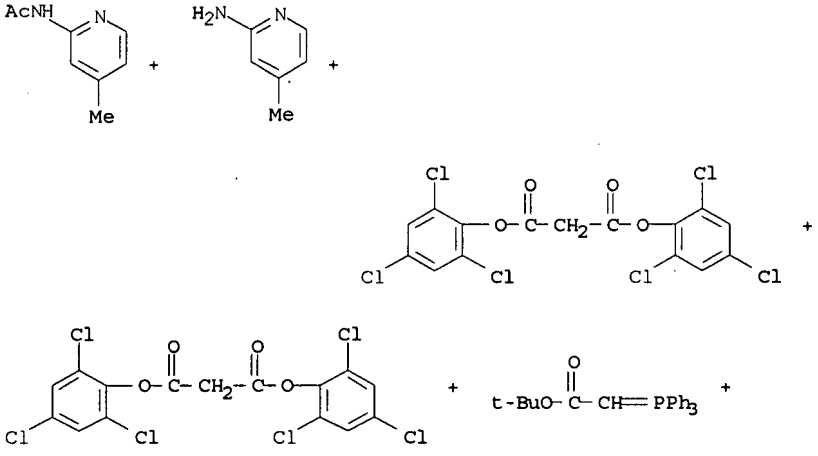


65%

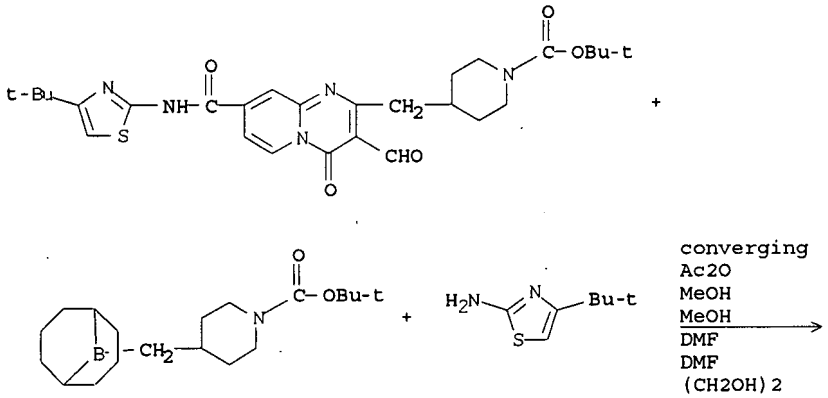
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(8) reflux
STEP(9) reflux
STEP(10) 1 hour, reflux
STEP(11.1) 40 minutes, 0 deg C
STEP(11.2) 1 hour, 80 deg C
STEP(12) 2 hours, reflux
STEP(13.1) 1 hour, reflux
STEP(13.2) room temperature; 4 hours, 60 deg C
STEP(14.1) 30 minutes, room temperature
STEP(14.2) room temperature, pH 4
STEP(15) 12.5 hours, room temperature
STEP(16) 1 hour, 0 deg C

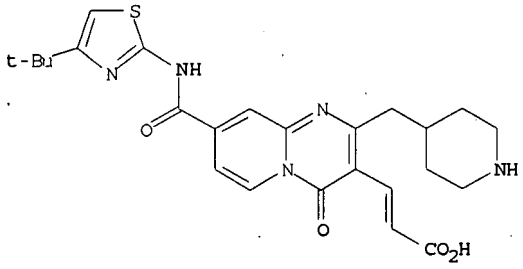
RX(529) OF 531 - 17 STEPS



RX(529) OF 531 - 17 STEPS



RX(529) OF 531 - 17 STEPS

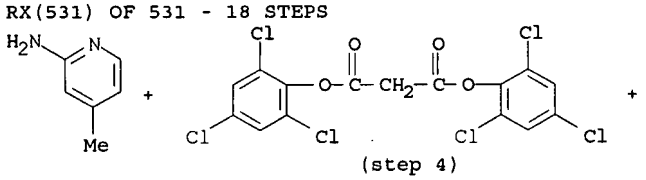


65%

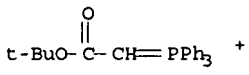
NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective

CON: STEP(1) reflux
STEP(2) reflux
STEP(3) 1 hour, reflux
STEP(4.1) 40 minutes, 0 deg C
STEP(4.2) 1 hour, 80 deg C
STEP(5) 47 hours, room temperature
STEP(6) 47 hours, room temperature
STEP(7) 30 minutes, room temperature
STEP(9) reflux
STEP(10) reflux
STEP(11) 1 hour, reflux
STEP(12.1) 40 minutes, 0 deg C
STEP(12.2) 1 hour, 80 deg C
STEP(13) 2 hours, reflux
STEP(14.1) 1 hour, reflux
STEP(14.2) room temperature; 4 hours, 60 deg C
STEP(15.1) 30 minutes, room temperature
STEP(15.2) room temperature, pH 4
STEP(16) 12.5 hours, room temperature
STEP(17) 1 hour, 0 deg C

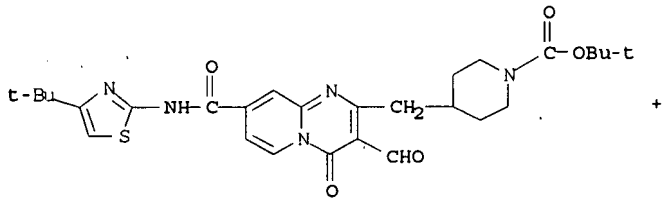
RX(531) OF 531 - 18 STEPS



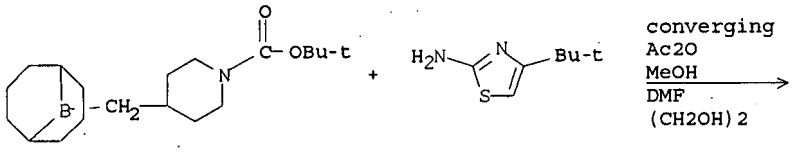
(step 4)



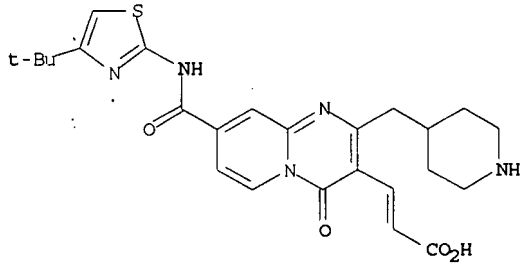
(step 6)



RX(531) OF 531 - 18 STEPS



converging
Ac2O
MeOH
DMF
(CH2OH)2



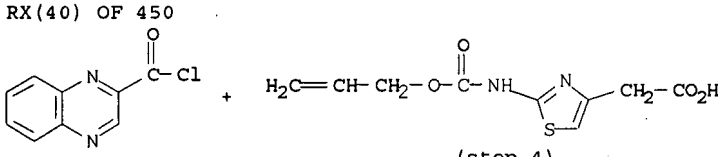
65%

NOTE: Vilsmeier-Haack reaction, Wittig reaction, stereoselective, Wittig reaction, stereoselective, Vilsmeier-Haack reaction, Suzuki-Miyaura reaction second stage, chemoselective
CON: STEP(2) reflux
STEP(3) reflux
STEP(4) 1 hour, reflux
STEP(5.1) 40 minutes, 0 deg C
STEP(5.2) 1 hour, 80 deg C
STEP(6) 47 hours, room temperature
STEP(7) 47 hours, room temperature
STEP(8) 30 minutes, room temperature
STEP(10) reflux
STEP(11) reflux
STEP(12) 1 hour, reflux
STEP(13.1) 40 minutes, 0 deg C
STEP(13.2) 1 hour, 80 deg C
STEP(14) 2 hours, reflux
STEP(15.1) 1 hour, reflux
STEP(15.2) room temperature; 4 hours, 60 deg C
STEP(16.1) 30 minutes, room temperature
STEP(16.2) room temperature, pH 4
STEP(17) 12.5 hours, room temperature
STEP(18) 1 hour, 0 deg C

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 143:359414 CASREACT
TI Discovery of hydroxamic acid analogs as dual inhibitors of phosphodiesterase-1 and -5
AU Dan, Akihito; Shiyama, Takaaki; Yamazaki, Kazuto; Kusunose, Naoto; Fujita, Katsuya; Sato, Hideshi; Matsui, Kazutaka; Kitano, Masafumi
CS Research Division, Sumitomo Pharmaceuticals Co., Ltd, 3-1-98 Kasugadenaka, Konohana-ku, Osaka, 554-0022, Japan
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(18), 4085-4090
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB HTS and the following synthesis of a series of the compds. led us to the discovery of hydroxamic acid analogs as potent dual inhibitors of phosphodiesterase (PDE)-1 and 5. These compds. have highly related structure and deviation of the structure usually resulted in reduced potency. This result can be used to design other mols. that may be utilized for the therapy of cardiovascular symptoms that relates to cGMP level.

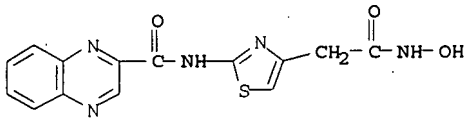
RX(40) OF 450



(step 7) (step 4)

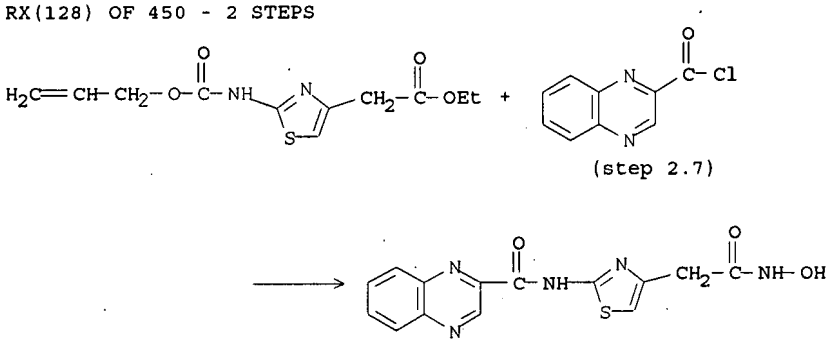
1. MeSO2Cl, R:119138-29-3, EtN(Pr-i)2, CH2Cl2
2. N-Hydroxyphthalimide, Cs2CO3, NMEP
3. N2H4, EtOH
4. i-PrN:C:NPr-i, DMF
6. Pd(PPh3)4, Morpholine, THF
7. i-PrN:C:NPr-i,

RX(40) OF 450



NOTE: combinatorial, solid-supported reaction(first stage treatment of Sasrin resin), reaction mixture from stage four treated with resin from stage three in stage five, reactant assumed seventh stage
CON: STAGE(1) 1 hour, room temperature
STAGE(2) 16 hours, 80 deg C
STAGE(3) 20 hours, room temperature
STAGE(4) 30 minutes, room temperature
STAGE(5) 16 hours, room temperature
STAGE(6) 18 hours, room temperature
STAGE(7) 18 hours, room temperature
STAGE(8) 3 hours, room temperature

RX(128) OF 450 - 2 STEPS



NOTE: 1) resin in H+ form second stage, 2) combinatorial, solid-supported reaction(first stage treatment of Sasrin resin), reaction mixture from stage four treated with resin from stage three in stage five, reactant assumed seventh stage
CON: STEP(1.1) 15 hours, room temperature
STEP(1.2) room temperature, neutralized
STEP(2.1) 1 hour, room temperature
STEP(2.2) 16 hours, 80 deg C
STEP(2.3) 20 hours, room temperature
STEP(2.4) 30 minutes, room temperature
STEP(2.5) 16 hours, room temperature
STEP(2.6) 18 hours, room temperature
STEP(2.7) 18 hours, room temperature
STEP(2.8) 3 hours, room temperature

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 13:18:28 ON 16 AUG 2007)

FILE 'CASREACT' ENTERED AT 13:18:42 ON 16 AUG 2007
L1 STR
L2 STR L1
L3 1 L2
L4 3 L2 FULL

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